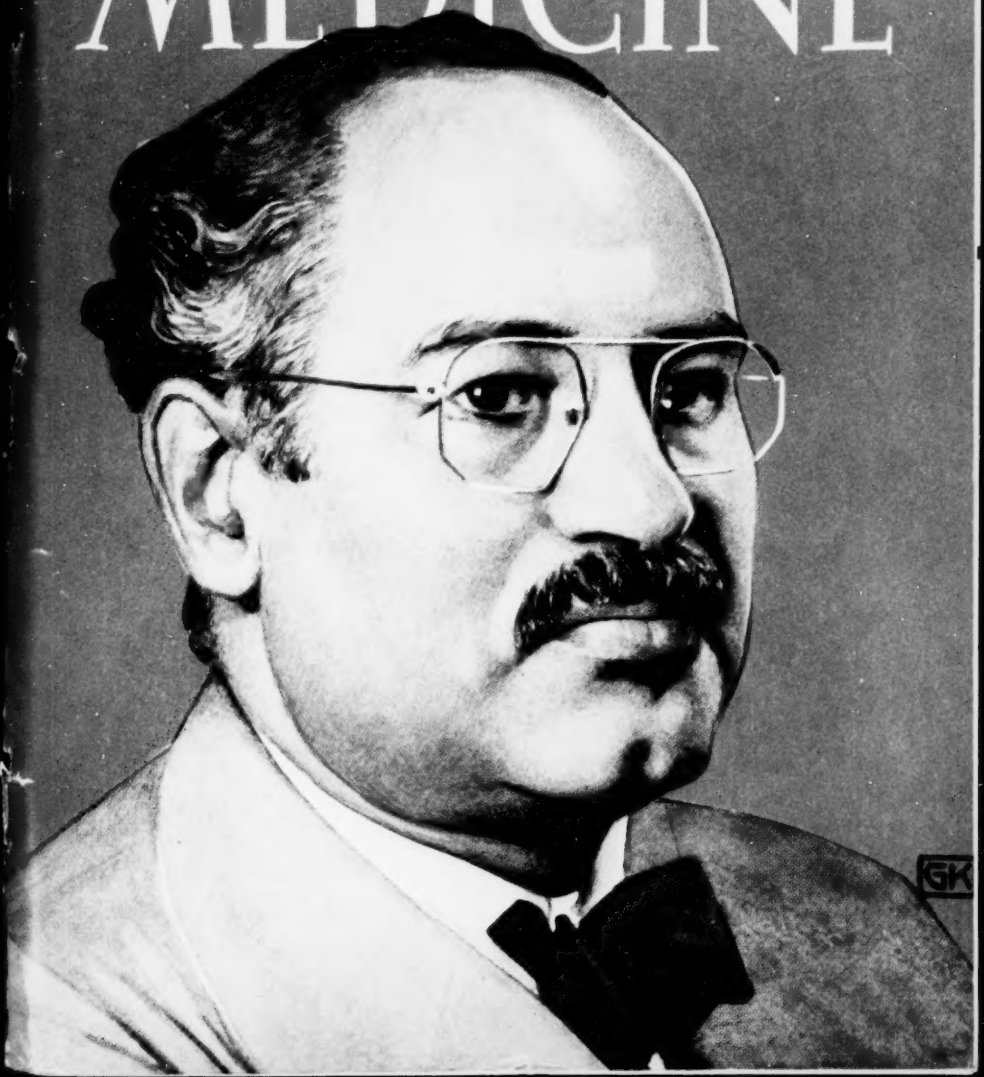
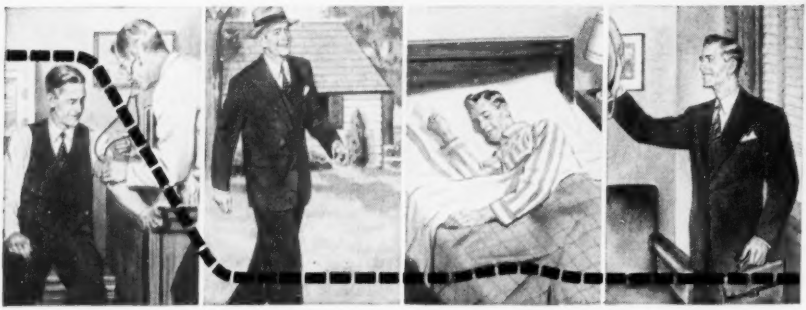
MAY 15, 1953

MODERN MEDICINE

The Journal of Diagnosis and Treatment



Isn't this the picture you want to prescribe for your hypertensive patients?



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And . . . therapeutic dosages of NITRANITOL can be maintained over long periods of time . . . *without* frequent checkups . . . *without* worry about possible toxic effects.

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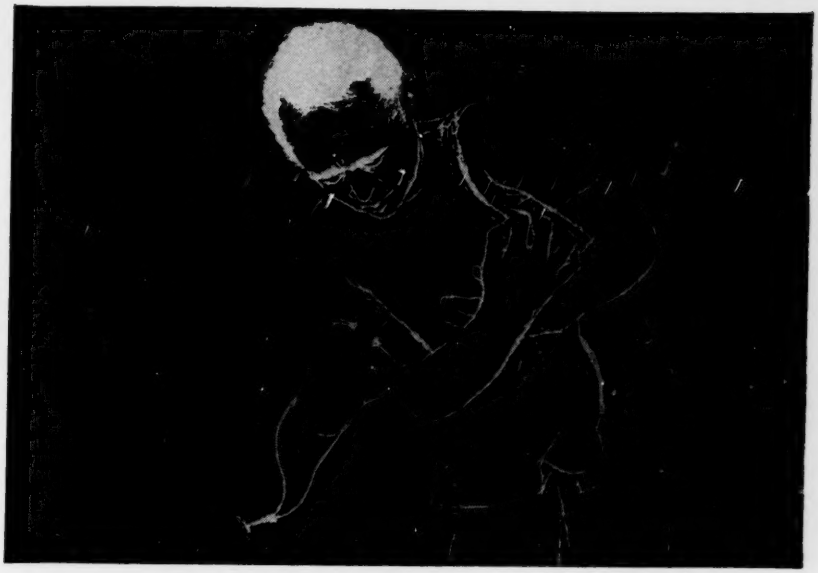
*alkavervir



to prevent attacks in angina pectoris

4 out of 5 patients respond in 3 studies

The consistency with which Peritrate can prevent attacks in angina pectoris is demonstrated in the published reports of three investigators. Each obtained good results in almost the same high percentage of patients:

Humphrey *et al.*[1] ...*78.4% fewer attacks*
Plotz[2] .....*80% fewer attacks*
Dailheu[3] .....*80% fewer attacks*

Used as a prophylactic agent — rather than to provide relief when an attack is present or imminent — Peritrate will in many cases

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- reduce the severity of attacks which are not prevented

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Extensive clinical use has demonstrated that, in addition to preventing or minimizing attacks, Peritrate will frequently

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For effective prophylaxis

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1. Humphreys, P., *et al.*: Angiology *3*:1 (Feb.) 1952. 2. Plotz, M.: N. Y. State J. Med. *52*: 2021 (Aug. 15) 1952. 3. Dailheu-Geoffroy, P.: L'Ouest-Méd., vol. 3 (July) 1950.

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MODERN MEDICINE

THE JOURNAL OF DIAGNOSIS AND TREATMENT

MODERN MEDICINE, The Journal of Medical Progress, of Minneapolis, Minn., is published twice monthly on the first and fifteenth of each month, at 55 East 10th Street, St. Paul 2, Minn. Subscription rate: $10.00 a year, 50c a copy.

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In pruritus ani

he is willing to try almost anything to obtain relief, but his troubles are not likely to be helped by

—ineffective calamine[1]

—irritating phenol[2]

—sensitizing local anesthetics of the "caine" group[3]

—antihistaminics which are known as "great sensitizers"[3]

his relief is assured

with non-sensitizing, effective CALMITOL. The ingredients of Calmitol—camphorated chloral, hyoscyamine oleate and menthol—raise the threshold of sensory nerve endings and skin receptors and promptly stop itching.

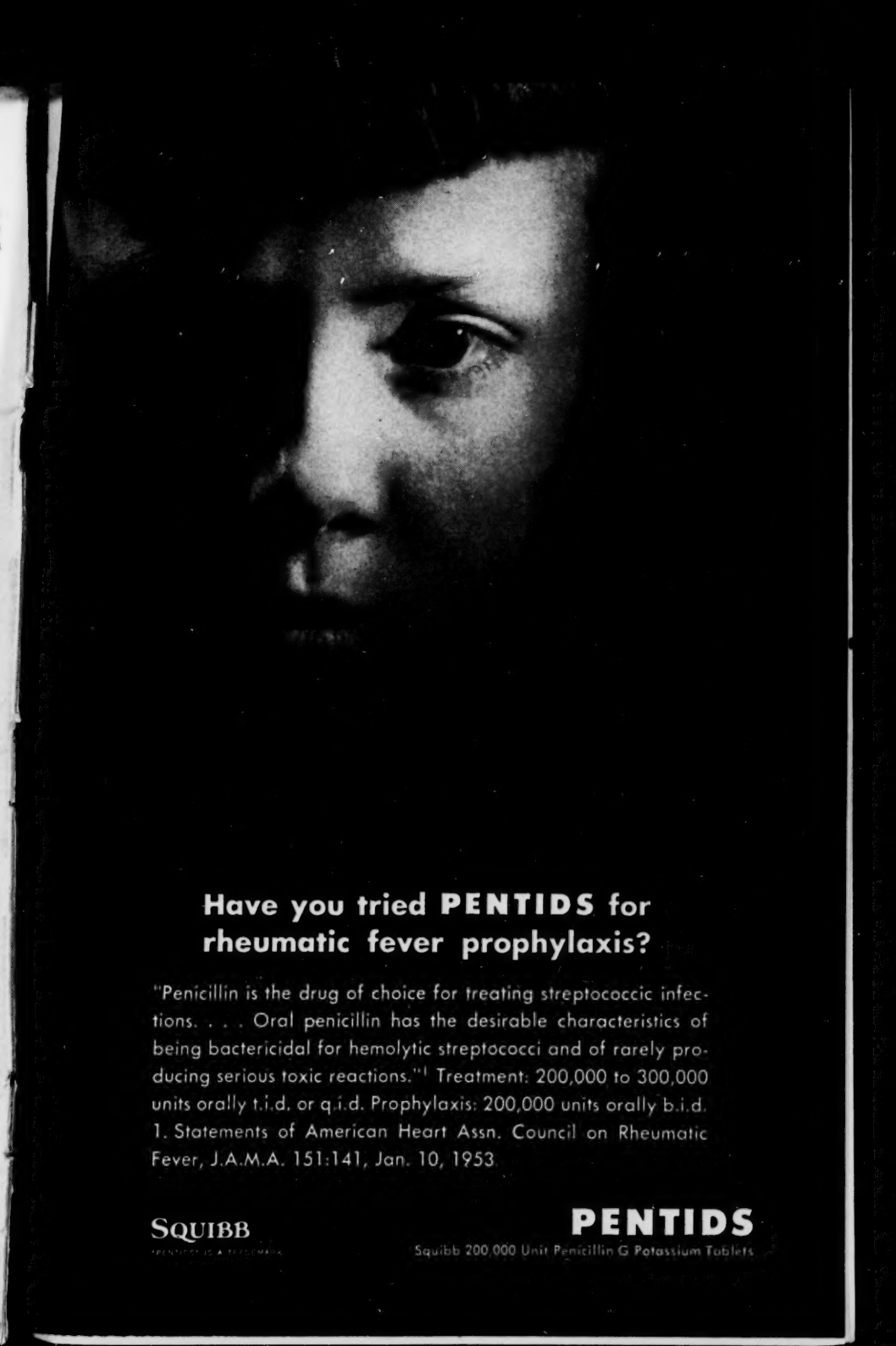
1. Goodman, H.: J.A.M.A. *129*:707, 1945.
2. Lubowe, I. I.: New York State J. Med. 50:1743, 1950.
3. Nomland, R.: Postgrad. Med. *11*:412, 1952.

the non-sensitizing antipruritic

Thos. Leeming & Co. Inc. 155 East 44th Street, New York 17, N. Y.

MODERN MEDICINE

THE JOURNAL OF DIAGNOSIS AND TREATMENT



Have you tried **PENTIDS** for rheumatic fever prophylaxis?

"Penicillin is the drug of choice for treating streptococcic infections. . . . Oral penicillin has the desirable characteristics of being bactericidal for hemolytic streptococci and of rarely producing serious toxic reactions."[1] Treatment: 200,000 to 300,000 units orally t.i.d. or q.i.d. Prophylaxis: 200,000 units orally b.i.d.

1. Statements of American Heart Assn. Council on Rheumatic Fever, J.A.M.A. 151:141, Jan. 10, 1953

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PENTIDS

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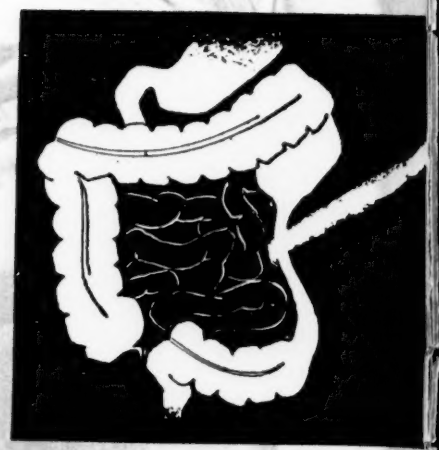
Efficient spasmolysis . . .



...in functional disorders

. . . such as irritable colon, emotional diarrhea, peptic ulcer, pyrosis; also for inflammatory diarrhea due to acute gastroenteritis or ulcerative colitis, and functional dysmenorrhea.

Elixir

BUTISOL® - BELLADONNA

—has a more definite, efficient antispasmodic action because it combines in each 5 cc. (one teaspoonful):

1 • BUTISOL® SODIUM 10 mg. (⅙ gr.)—"intermediate sedative" which is "particularly useful in the field of daytime sedation."[1] The mild, relatively prolonged action of Butisol Sodium "makes it suitable for management of many functional disorders."[1]

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...in an exceptionally pleasant-tasting elixir colored an appetizing orange-red. Supplied in bottles of one pint and one gallon. Samples on request.

1. Dripps, R. D.: Selective Utilization of Barbiturates, J.A.M.A. 139:148 (Jan. 15) 1949.

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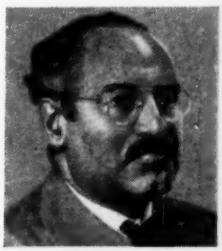
for
May 15
1953

Modern Medicine
Vol. 21, No. 10

THE MAN ON THE COVER is Dr. Abner I. Weisman of New York City, Associate in Obstetrics and Gynecology at New York Medical College and guest editor of the Symposium on Fertility and Sterility beginning on page 79. Dr. Weisman is associate attending obstetrician and gynecologist at Jewish Memorial Hospital and associate visiting obstetrician and gynecologist at the Metropolitan Hospital. Managing editor of *Fertility and Sterility*, Dr. Weisman is author of *Spermatozoa and Sterility*. A member of the Association for the Study of Internal Secretions, Dr. Weisman is a founding member of the American Society for the Study of Sterility, the International Fertility Association, and the New York Fertility Society.



Contents for May 15 1953

CONTINUED

in allergic rhinitis and sinusitis

. . . secondary infections associated with allergic states

NEW DIFFERENT

Biomydrin* nasal spray contains Thonzonium Bromide††

Thonzonium bromide is Nepera's exclusive **bactericidal wetting agent** that provides spreading and penetrating power for all the active therapeutic substances contained in BIOMYDRIN.

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†Busis, S. N., and Friedman, L. L.: Antibiotics & Chemotherapy 3:299 (March) 1953.

Contents for May 15 1953

CONTINUED

Business Manager: M. E. Herz.

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LETTER FROM THE EDITORS

Dear Reader:

Science knows no political boundaries. Developments in medicine belong to the world. This has always been a basic concept in our editorial philosophy.

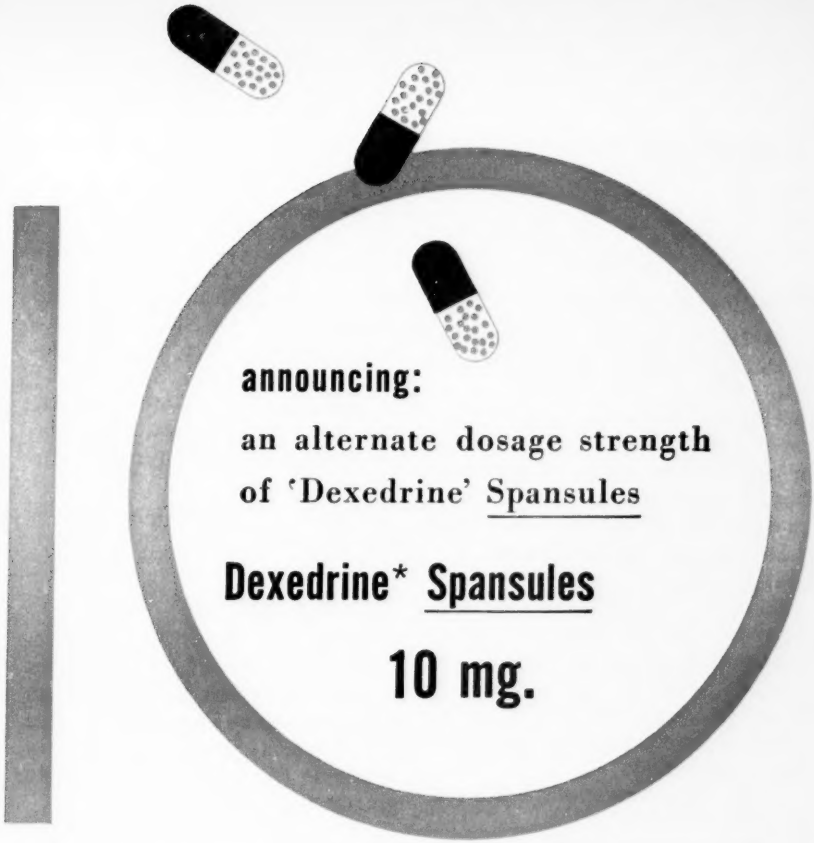
The man of science, and in this respect the physician, is no different from the rest, is not content with knowing only what is going on in his own bailiwick. He wants to know what the scientists everywhere and anywhere are doing about the problems that are engaging him.

In an endeavor to satisfy in part this questing curiosity, *Modern Medicine* has inaugurated a new department called "Short Reports from Abroad." Extraordinary efforts are being made to bring to your attention items of medical interest from foreign lands. This coverage is in addition to the regular reporting of progress in countries other than our own, which has always been an important feature of the editorial service of *Modern Medicine*.

In this issue (page 194) the new department takes you to Great Britain, France, Germany, and Argentina. In the short time since the first appearance of "Short Reports from Abroad" items have been reported from 3 continents.

The department was introduced into *Modern Medicine* without fanfare. No announcement was made. None was needed. Your response was immediate and enthusiastic. It proves again that the range of the physician's interest is world wide.

The Editors



So that you will be able to prescribe the strength of 'Dexedrine' *Spansules* that best suits the individual patient, S.K.F. has now introduced 'Dexedrine' *Spansules* 10 mg. as an alternate to the original 15 mg. dosage strength.

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1. sustained and prolonged appetite curbing effect
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Correspondence

Communications from the readers of MODERN MEDICINE *are always welcome. Address communications to The Editors of* MODERN MEDICINE, *84 South 10th St., Minneapolis 3, Minn.*

Musculoskeletal Pain

TO THE EDITORS: The comments of Dr. Jed H. Irvine *(Modern Medicine,* Mar. 1, 1953, p. 20) serve to emphasize the controversial aspects of the interpretation and management of rheumatic diseases. Obviously, the principal point of interest is the relief of pain, which is also the chief reason for the patient to seek medical aid.

Some of my viewpoints on this type of painful condition have been published *(Modern Medicine,* Nov. 15, 1952, p. 18). More detailed discussion is contained in a recent paper in *Journal-Lancet* (73:63-68, 1953).

From my observations, I am led to believe that:

1] The commonest clinical form of musculoskeletal pain is caused by a pathologic lesion occurring at one, or both, of two sites in the lower portion of the back.

2] From these two sites, referred phenomena—pain and tenderness—can be transmitted to many other parts of the body.

3] Three distinct pain syndromes may develop, singly or combined, from the pathologic lesions.

4] Autonomic concomitants may be derived from the afferent impulses; they probably represent many of the clinical manifestations interpreted as psychosomatic diseases, although actually somatopsychic in sequence.

5] The entire chain of manifestations can be eliminated by a relatively simple surgical procedure at the site of origin.

R. J. DITTRICH, M.D.

Duluth

Excellent Exhibit

TO THE EDITORS: Are any reprints available of the excellent Special Exhibit on Immune Serum Globulin which appeared in the March 15, 1953 issue of *Modern Medicine* (p. 102)? If so, I would greatly appreciate 3 reprints.

LOUIS A. SCHNEIDER, M.D.

Fort Wayne

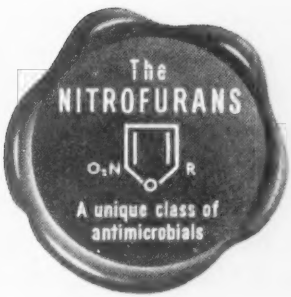
¶ Sorry. Reprints are not available.—Ed.

Relief from Migraine

TO THE EDITORS: I have been observing such excellent results in the treatment of severe resistant migraine with Mercuhydrin that I thought a preliminary report might stimulate inquiry by qualified investigators.

Campbell, Hay, and Tonks, in the *British Medical Journal* in De-

news.....

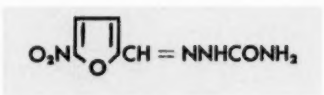


news of an important advance in chemotherapy

A DRAMATIC CHAPTER in medicine opened unexpectedly in recent years with the discovery of powerful antimicrobial agents which had highly specific action against bacteria—with but little toxicity for human tissues.

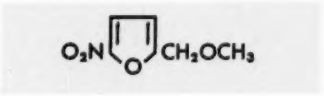
Among the few classes of drugs yet included in this category are the sulfonamides, antibiotics and the nitrofurans.

Discovered at Eaton Laboratories in 1939, the powerful antimicrobial action of these nitrofurans was accompanied by several fundamental advantages: a wide antibacterial spectrum, low cytotoxicity, negligible development of bacterial resistance, stability and a simplicity of chemical structure which permits ready synthesis of numerous variations.

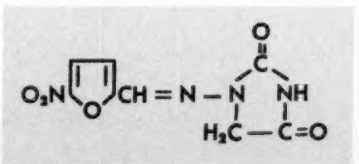


Soon following this basic discovery, *the first nitrofuran was elaborated for clinical use.* This was *Furacin,* brand of nitrofurazone N.N.R., the topical antibacterial agent.

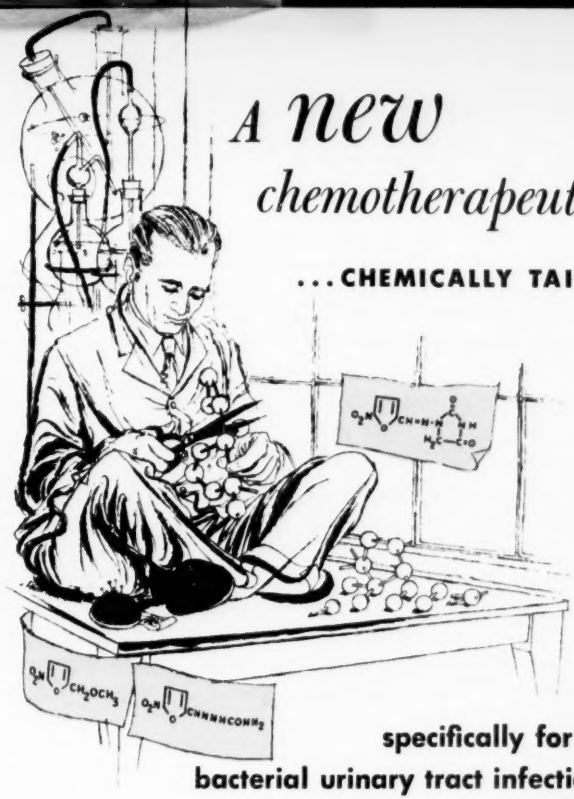
Continued chemical syntheses and bacteriologic assays next revealed a *second nitrofuran* with antifungal properties: *Furaspor,* brand of nitrofurfuryl methyl ether. This has been employed clinically as a topical fungicide.



As information accumulated concerning the exact mode of antimicrobial action of these compounds and their catabolism in the body, organic chemists tailored these nitrofuran molecules to fit the specifications for a systemic antibacterial agent, involving such factors as rapid bactericidal action, solubility, stability, absorption, catabolism and excretion.



An important degree of success has now been attained in the form of the *third* nitrofuran produced for clinical use—*the first designed for systemic administration:* **Furadantin.**



A new chemotherapeutic molecule

...CHEMICALLY TAILORED...

specifically for refractory bacterial urinary tract infections:

PYELONEPHRITIS
PYELITIS
CYSTITIS

with definite advantages:

FURADANTIN®

- clinical effectiveness against most of the bacteria of urinary tract infections, *including many strains of Proteus, Aerobacter and Pseudomonas species.*
- low blood level—bactericidal urinary concentration
- effective in blood, pus and urine—independent of pH
- limited development of bacterial resistance
- rapid sterilization of the urine
- oral administration
- stable
- low incidence of nausea—no diarrhea or abdominal pain—no proctitis or pruritus—no crystalluria or hematuria
- nonirritating—no cytotoxicity—no inhibition of phagocytosis
- tailored specifically for urologic use

CLINICAL EFFECTIVENESS

of Furadantin *in urinary tract infections:*

● **FURADANTIN HAS PROVED ESPECIALLY EFFECTIVE** in refractory Proteus infections. It produced complete clinical and bacteriologic cures in 14 of 22 patients with acute or chronic cystitis or pyelonephritis due to Proteus species. Definite symptomatic improvement was obtained in the remainder, without a single failure. *All of these patients had been previously treated unsuccessfully with various antibiotics.* Furadantin dosage was 5 to 10 mg. per Kg. per day, depending on the susceptibility of the patient to nausea. In no case did nausea or emesis require termination of treatment and there was no instance of sensitization, diarrhea, pruritus or proctitis (1).

● **THIRTY-THREE AMBULATORY PATIENTS** with acute or chronic pyelonephritis or cystitis were treated with Furadantin. Of these, 17 were cured both clinically and bacteriologically, 14 were improved and only 2 were failures. Most patients required only 5 days of treatment. Among the bacteria eradicated were 16 of 22 strains of E. coli, 4 of 6 strains of A. aeruginosa, 3 of 5 strains of Proteus species and 1 of 3 strains of Pseudomonas aeruginosa. Nausea and occasional emesis were controlled successfully in all cases by reduction of dosage below the usual range of 7 to 9 mg. per Kg. No other untoward effects were observed (2).

● **IN A THIRD STUDY** Furadantin was administered to over 70 persons. One group of 12 patients with chronic, miscellaneous urinary tract infections had failed to respond to other modern antibacterial therapy. Of these, 5 were completely cured, 3 were improved and 4 were failures. Bacteria eradicated included Pseudomonas, E. coli, A. aerogenes and enterococci. Furadantin dosage was 7 mg. per Kg. for 14 days.

Of 59 persons receiving doses of 5 to 7 mg. per Kg., nausea occurred in only 2. Among the 79 subjects and patients on clinical dosage levels for as long as 14 days, there was no case of sensitization, blood dyscrasia, proctitis, anal pruritus, crystalluria, abdominal pain or diarrhea (3).

1. Friedgood, C. E., and Danza, A.: ***Furadantin in Urinary Tract Infections Due to Proteus.*** Read at the Clinical Congress of the American College of Surgeons, New York City, September, 1952.

2. Norfleet, C. M., Jr.; Beamer, P. R., and Carpenter, H. M.: ***Furadantin in Infections of the Genitourinary Tract.*** Read at the Annual Meeting of the Southeastern Section of the American Urological Association, Boca Raton, April, 1952.

3. Mintzer, S.; Kadison, E. R.; Shlaes, W. H. and Felsenfeld, O.: ***Treatment of Urinary Tract Infections with a New Antibacterial Nitrofuran,*** Antibiotics and Chemotherapy *3* (Feb.) 1953.

FURADANTIN DOSAGE

Accurate dosage based on body weight is important to minimize nausea.

The average dose is 5 to 8 mg. per Kg. (2.2 to 3.6 mg. per lb.) body weight nude per 24 hours. One-fourth of this dose is administered with each meal and on retiring. Cold milk or food should be given with the last dose at night to prevent nausea. Therapy is continued for at least 3 days after the urine becomes sterile.

For resistant infections, as by Proteus, Aerobacter or Pseudomonas, the dose may be increased to the maximum of 10 mg. per Kg. per day (4.5 mg. per lb.).

Do not administer Furadantin for more than 14 consecutive days. If there is a recurrence of infection, allow a 4 week rest period before resuming therapy.

Until more clinical data are obtained, Furadantin is not yet recommended for young children. Its use is contraindicated in anuria, oliguria, or severe renal damage. It cannot replace essential surgery.

CAUTION: Since this is a new drug, its use should be confined, for the present, to serious infections that are not amenable to other agents.

As with all new and powerful chemotherapeutic agents, it is recommended that routine blood cell studies be made during treatment. The clinician should always be alert for possible sensitization and other untoward systemic reactions.

This dosage chart permits administration of one size tablet only

Body Weight		Dosage Range mg./Kg./24 hours		Average Dose with meals and at bedtime	
Pounds	Kg.	from	to	No. tab.	Size tab.
60-84	27-38	7.3	5.2	1	50 mg.
85-114	38-51	7.7	5.8	1½	50 mg.
115-139	52-63	7.6	6.3	1	100 mg.
140-169	64-76	7.8	6.5	2½	50 mg.
170-224	77-101	7.7	5.9	1½	100 mg.
225-250	102-113	7.8	7.0	2	100 mg.

FURADANTIN *is* . . .

brand of nitrofurantoin [N-(5-nitro-2-furfurylidene)-1-aminohydantoin], a crystalline yellow compound of bitter taste, slightly soluble in water. It is readily absorbed from the alimentary tract and about 40 per cent is excreted in the urine. Its solubility in urine is such as to obviate all danger of crystalluria. Furadantin is stable in storage and to all physiologic pH values. The oral LD_{50} in mice is 895 mg. per Kg.

Its antibacterial spectrum in vitro against urinary tract organisms includes many strains of:

GRAM-NEGATIVE

Aerobacter aerogenes
Escherichia coli
Neisseria gonorrhoeae
Pasteurella multocida
Proteus vulgaris
Paracolobactrum species
Pseudomonas aeruginosa
Salmonella choleraesuis
Salmonella enteritidis
Salmonella paratyphi
Salmonella schottmülleri
Salmonella typhimurium
Salmonella typhosa
Shigella dysenteriae
Shigella paradysenteriae
Vibrio comma

GRAM-POSITIVE

Corvnebacterium diphtheriae
Corynebacterium species (diphtheroids)
Micrococcus (Staph.) pyogenes var. aureus and albus
Streptococcus faecalis
Streptococcus pyogenes (hemolyticus)
Streptococcus mitis

Scored yellow tablets of

50 mg. in bottles of 50 & 250.
100 mg. in bottles of 25 & 250.

Available through your pharmacy and hospital on prescription.

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The NITROFURANS
A unique class of antimicrobials

cember 1924, reported a sudden elevation of blood sodium at the onset of an attack of migraine and a sudden lowering of blood sodium when the attack terminated.

For several months I have been using 0.5 to 1 cc. of Mercuhydrin intramuscularly. There have been no failures in a small series. Within about two hours, not only is the headache gone, but also the important associated feelings of tension over the scalp and face and burning of the eyes. No nausea results from the treatment as is common with vasoconstrictor drugs.

The relief is usually so complete that the patient is ready to go back to work.

ROBERT S. SRIGLEY, M.D.
Hollis, Okla.

Beer a Red Herring?

TO THE EDITORS: The Visiting M.D. in Diagnostix Case MM-234 (*Modern Medicine,* Mar. 1, 1953, p. 169) states that the consumption of 6 bottles of beer a day for twenty-five years is a red herring regarding the causal relation to alcoholism and cirrhosis of the liver.

I would like to know the opinions of internists about the country on just how much alcohol, if any, is related to cirrhosis of the liver.

If 6 bottles of beer a day for twenty-five years has no relation, it is pretty safe to say there is no relation between alcohol and cirrhosis of the liver.

LOUIS KEATING, M.D.
Yonkers, N. Y.

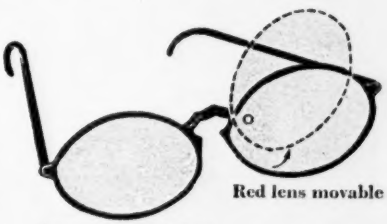
¶ Do other readers have any ideas on this subject?—Ed.

Ocular Accommodation to Dark

TO THE EDITORS: I would like to present an idea which you might want to publish in your magazine.

Through experimentation, I have found that one can accommodate for night vision with one eye. Several other doctors who use the fluoroscope frequently have found the idea convenient. It is especially useful when one has to see a film or do some procedure which is difficult when looking through red glasses.

One eye is protected with either a blackened lens or the accommodation glasses and the other lens is



made so that it is movable (see illustration).

When the uncovered eye is used in daylight the covered eye retains the accommodation.

SAMUEL L. COHEN, M.D.
Bellflower, Calif.

Urine for Pregnancy Test

TO THE EDITORS: My attention has been called to the question about pregnancy tests and pregnancy hormones (*Modern Medicine,* Mar. 1, 1953, p. 33).

Since there are inaccuracies in the answer, I should like to take

this opportunity to correct them. I feel that I am expertly qualified, since I am the codiscoverer of the Frank-Berman rat pregnancy test.

My corrections are as follows:

- Collect all voidings during normal sleeping time plus voiding on arising.
- Do not restrict fluid intake of the patient in order to concentrate urine. Concentrated urine will either kill the animal or make it difficult to read ovaries. Hormones, Prostigmin, antihistamines, sulfonamides, laxatives, quinine, and ergot should be avoided for ninety-six hours before the collection of the urine. No alcoholic beverages should be drunk for twenty-four hours before collection.
- The bottle in which urine is submitted should be clean.
- Specimens mailed to a laboratory should be packed in dry ice. No preservative is to be added to urine.
- Specimens must be kept under constant refrigeration; the gonadotropic hormone may be destroyed in a few hours if not refrigerated.
- The *p*H of urine is not tested. No acid is to be added to urine.
- Urines are never filtered but centrifuged to bring phosphates, urates, white blood count, crystals, epithelial cells, and so on. Clear supernatant urine is used. If a patient who is bleeding is instructed to insert a Tampax before collection of urine, no blood need appear in urine sample. Toxic specimens cannot be detoxified by ether. No glucose is added to the urine.
- Urine is kept at room temperature for one-half hour before injecting to remove chill. No specific gravity is taken.

ROSE L. BERMAN

New York City

Iodine for Diarrhea

TO THE EDITORS: I thought you might be interested in our use of iodine in the control of diarrhea caused by terramycin or aureomycin. The overgrowth of *Monilia* seems a possible cause of the diarrhea: therefore, the use of iodine.

We prescribe the iodine as Diodoquin, 10 gr. three times a day, often in conjunction with the terramycin or aureomycin. Use after diarrhea has started is usually successful.

ALBERT H. ROWE, M.D.
Oakland, Calif.

Penicillin Anaphylaxis

TO THE EDITORS: The frequency of severe anaphylactic reactions to penicillin, including fatalities, is apparently increasing rapidly. In a little more than a year, 15 instances have been published, of which 6 were fatal. In New York City and vicinity I have been informed of at least 9 additional cases, 4 fatal.

The problem of preventing these serious reactions is difficult, and the complete prevention may not be possible at present. However, the following points concerning anaphylactic shock after penicillin may be noted:

- Anaphylaxis occurs only in patients who have had penicillin previously, usually on several occasions. The history of previous penicillin exposure may be erroneous because some patients receive the drug without knowing it, for example, as troches or by inhalation.
- Anaphylaxis can occur even though penicillin was well tolerated previously.
- Anaphylaxis is more frequent in allergic individuals and is more likely

(Continued on page 24)

FOR THE *Pediatric Patient* WHO WILL NOT DRINK MILK!

CARBONATED BEVERAGE "SODAS"

If the mothers of your pediatric patients have this problem, doctor—here's a possible solution.

Why not suggest a third-glass of chilled evaporated milk into which is poured two-thirds of a glass of a carbonated beverage—any flavor the young patient desires. To solve the problem of the amount of milk the child requires, the drink may be taken between meals as well. Appetite will not be depressed owing to the pleasant stimulation of the taste buds by the carbonated beverage.

Flavors may be rotated to keep up the child's interest. The sugar content (largely invert) is just enough to keep the little one happy and help provide quick energy. The carbonation may be relied upon to help empty the stomach. Clinical research has confirmed that carbonated beverages do not injure teeth.

Carbonated beverages are suggested only as a suitable supplement to the basic dietary recommendations of the Food and Nutrition Board of the National Research Council.

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[ORAL FAT EMULSION SCHENLEY]

caloric boost *without* gastric burden

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12 pats of butter, or
1 dozen Parker House rolls, or
6 servings of macaroni and cheese, or
8 boiled eggs, or
6 baked potatoes, or
9½ slices of bread

The unusually small particle size of EDIOL* (average, 1 micron) favors ease of digestion, rapid assimilation. Prepared from vegetable oil (50%) and sucrose (12½%), EDIOL can be taken by tasty spoonfuls; in milk or fruit juices; on fruits, puddings, or desserts.

At all pharmacies, in bottles of 16 fl. oz. For children, or where fat tolerance may be a problem, small initial doses may be prescribed and gradually increased to level of individual tolerance.

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to be fatal in asthmatics. However, it may occur without such a history.

• The dangerous and potentially shocking dose of the antibiotic is the first injection given following an interval since the last exposure. This interval has often been one of several months. This is comparable to animal experiment in which adequate spacing of antigen injections greatly enhances the likelihood of inducing shock. Subsequent successive doses probably are not dangerous. The precautions suggested are to be taken especially for this initial dose.

The following precautions are suggested to prevent anaphylaxis:

1] Avoid needless sensitization through the casual use of penicillin for trivial or doubtful indications: for example, troches, dust inhalations, and nose drops.

2] For mild infections, other chemotherapy or oral penicillin is preferable. While collapse from a penicillin tablet has apparently occurred, no deaths have been reported.

3] Take a careful history of penicillin treatment and reactions, and also of allergy and asthma. Particular attention must be paid to the timing of previous penicillin reactions following injection or ingestion. Thus *accelerated* and especially *immediate* reactions, no matter how mild, occurring minutes or hours after, are very significant, indicating the likelihood of anaphylaxis. Also important is the occurrence of more than one reaction, unusual reactions such as severe angioneurotic edema and bullous or purpuric eruptions, or allergic responses to simple contact or inhalation as seen in doctors, nurses, and others who handle or administer penicillin.

4] Preliminary tests may be helpful in screening out some of the

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This is possible with AMINODROX because gastric disturbance is avoided.

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Aminodrox Tablets contain 1 1/2 gr. aminophylline with 2 gr. activated aluminum hydroxide.

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Also available with 1/4 gr. phenobarbital.

violent reactors. A scratch test carried out with aqueous procaine penicillin in the usual treatment strength, 300,000 units per cubic centimeter, may well be done routinely. The test site should be observed closely, the solution being wiped away as soon as itching or reaction is definite. It is best to wait twenty minutes before considering the reaction negative. Intracutaneous tests may be dangerous and may be done only after a negative scratch test. If the scratch test seems negative, an additional precaution would be the administration of a 50,000-unit tablet of penicillin, waiting ten minutes before the injection of the antibiotic. A clearly positive scratch test reaction should in itself rule out penicillin administration.

5] Modification of the technic of penicillin injection is an additional precaution. The first or potentially shocking injection should be given into the arm rather than the buttock to permit application of a tourniquet if necessary. Avoid scrupulously the possibility of accidental intravenous injection. It may be wise to inject the first drop or two, then pause for forty-five seconds before completing the injection. The extremely rapid fatal reactions often make themselves evident within this period. Keep epinephrine directly at hand.

SHEPPARD SIEGAL, M.D.
New York City

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(1) Youmans, J. B., in Handbook of Nutrition, Chicago, American Medical Association, 1951, p. 577; (2) Hansen, A. E., in Mitchell-Nelson Textbook of Pediatrics, ed. 5, Philadelphia, W. B. Saunders Co., 1950, p. 106; (3) Heck, F. J.: J.A.M.A. 148: 783, 1952.

0.6 cc. contains 75 mg. (about 1 grain) ferrous sulfate. Available in 15 and 50 cc. bottles with calibrated dropper.

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ESTIVIN relieves ocular and nasal discomfort caused by hay fever. General conjunctivitis is also readily alleviated with ESTIVIN.

ESTIVIN is an aqueous infusion of "rosa gallica L." It is decongestive and soothing to irritated ocular and nasal membranes.

Dosage:

One drop of ESTIVIN in each eye will alleviate ocular and nasal discomfort and inhibit the production of irritating fluids.

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Sulfadiazine.....0.167 Gm.
Sulfamerazine.....0.167 Gm.
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Each Tablet or teaspoon (5 cc.) of suspension provides 0.5 Gm. of total sulfonamides.

Supplied: Deltamide tablets in bottles of 100; Deltamide Suspension in 4 oz. and 16 oz. bottles.

Indicated in infections due to Group A hemolytic streptococci, staphylococci, pneumococci, meningococci, gonococci, and other microorganisms responsive to sulfonamides.

1. Lehr, D.: Brit. M. J.: 2: 543-548, 1948.
2. Lehr, D.: Brit. M. J.: 2: 601, 1950.
3. Hawking, F., and Lawrence, J. S.: The Sulfonamides, New York, Grune and Stratton, 1951.

DELTAMIDE—a quadruple sulfonamide tablet and suspension—represents the latest development in multiple sulfonamide therapy. Deltamide utilizes the fact that an increase in the number of sulfonamides in sulfonamide mixtures provides the significant advantages of greater clinical safety with lowered incidence of toxic and allergic reactions.[1, 2]

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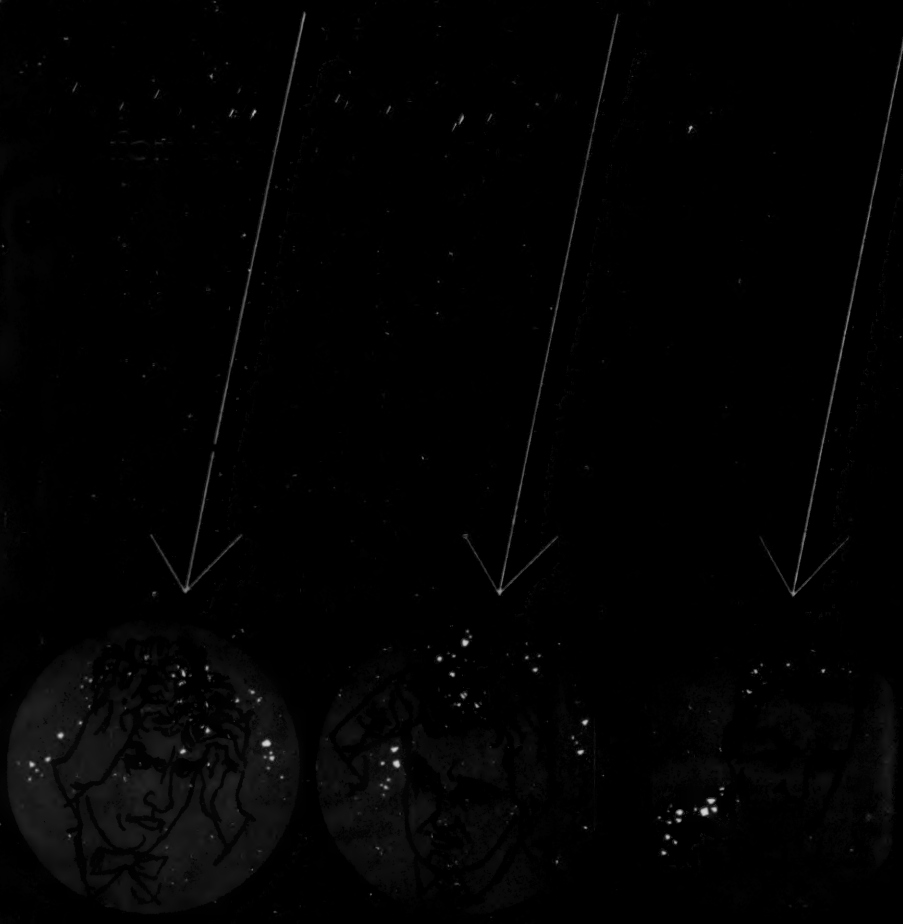

who have Seborrheic Dermatitis of the scalp . . . prescribe

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Effective control of scaling . . . prompt relief of itching and burning . . . extreme simplicity of use . . . this is the story of SELSUN Sulfide Suspension, Abbott's new *prescription-only* product for the management of seborrheic dermatitis of the scalp. Clinical investigators who treated 400 patients[1, 2, 3] found SELSUN effective in 92 to 95 percent of cases of mild seborrhea (common dandruff), and in 81 to 87 percent of all cases of seborrheic dermatitis.

SELSUN was successful in many cases that had failed to respond to other recognized methods of treatment. Optimum results were obtained in four to eight weeks, although itching and burning stopped after the second or third application in most cases. After the initial treatment period, a single application keeps the scalp free of scales for one to four weeks.

SELSUN is convenient to use, because it is simply applied while washing the hair and then rinsed out. It thus leaves the hair clean and odorless, and obviates the problem of stains on clothing and linens. Specific research on toxicity[1, 2] shows there are no harmful effects from external use of SELSUN as recommended. Supplied by pharmacies in 4-fluidounce bottles, with tear-off labels. Dispensed only on a physician's prescription. Abbott

References:

1. Slinger, W. N., and Hubbard, D. M. (1951), Arch. Dermat. & Syph., 64:41, July.
2. Slepyan, A. H. (1952), Ibid., 65:228, February.
3. Ruch, D. M. (1951), Communication to Abbott Laboratories.

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SULFIDE *Suspension*
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Questions & Answers

All questions received will be answered by letter directed to the petitioner; questions chosen for publication will appear with the physician's name deleted. Address all inquiries to the Editorial Department, MODERN MEDICINE, *84 South Tenth Street, Minneapolis 3, Minnesota.*

QUESTION: Is it true that a dilated common bile duct of blue coloration need not be explored?

M. D., Washington

ANSWER: *By Consultant in Surgery.* The statement that a dilated common bile duct of blue coloration need not be explored is completely erroneous. Inflammation of the bile duct over a period of time thickens the duct wall so that the duct wall becomes less transparent and the color is less influenced by the bile within the duct. However, a thin-walled duct may contain stones and should be explored when properly indicated.

QUESTION: What is the present conservative management of chronic cystic mastitis?

M.D., California

ANSWER: *By Consultant in Obstetrics & Gynecology.* Chronic cystic mastitis requires no treatment unless the symptoms are disabling or severe. If severe premenstrual breast pain occurs, the patient should wear a good uplift brassiere day and night until symptoms subside. If this is not sufficient, hormonal treatment consisting of progesterone buccal tablets, 10 mg. twice a day for a week premenstrually, should be tried and is often helpful. Any lump that feels different from the surrounding tissue should be removed for biopsy. Pregnancy frequently is helpful in improving the process and may lead to resolution of the cystic areas.

QUESTION: Occasionally we have heard most unusual heart murmurs in males during routine preemployment physical examinations. The heart, because of either fear or emotional distress, assumes a rapid rate and the sounds resemble the squeak of new leather. How are these murmurs formed?

M.D., Arkansas

ANSWER: *By Consultant in Cardiology.* A definite systolic murmur can be produced in many normal individuals when the heart rate is accelerated by exercise or emotion. The increase in vigor or quickness of ejection is probably responsible rather than the increase in rate.

Respiration may also be a factor in producing murmurs. With normal inspiration and expansion of the lungs, a greater amount of tissue intervenes over the precordium and may form a cushion against which the systolic beat of the heart may exert rhythmic contact, producing an extracardiac murmur.

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Given in proper dilution slowly by vein, Solution Intravenous Veriloid usually reduces both the systolic and diastolic blood pressures in a matter of minutes—entirely within the control of the physician. This valuable emergency drug frequently proves to be a life-saving measure. Contains 0.4 mg. of alkavervir (mixed Veratrum viride alkaloids) in 0.25 per cent acetic acid solution.

The dependable hypotensive response produced by Solution Intramuscular Veriloid quickly relieves the distressing symptoms of critically elevated blood pressure. Injected deep into a muscle, a single dose of Solution Intramuscular Veriloid leads to a significant fall in blood pressure. Attaining its maximum effect in 60 to 90 minutes, this drop persists for 3 to 6 hours. Through repeated injections, the tension may be kept depressed for many hours or even days if necessary.

During this period, continuous relief is afforded the patient. Thereafter, suitable oral medication should be given in an effort to maintain the relief so achieved.

Solution Intramuscular Veriloid is widely indicated in all types of severe hypertension:

- hypertensive states accompanying cerebral vascular disease
- malignant hypertension
- hypertensive crisis (encephalopathy)
- toxemias of pregnancy
- pre-eclampsia
- eclampsia

Solution Intramuscular Veriloid, providing 1.0 mg. of alkavervir (mixed Veratrum viride alkaloids) per cc. of isotonic buffered aqueous solution incorporating one per cent procaine hydrochloride, is supplied in 2 cc. ampuls in boxes of 6.

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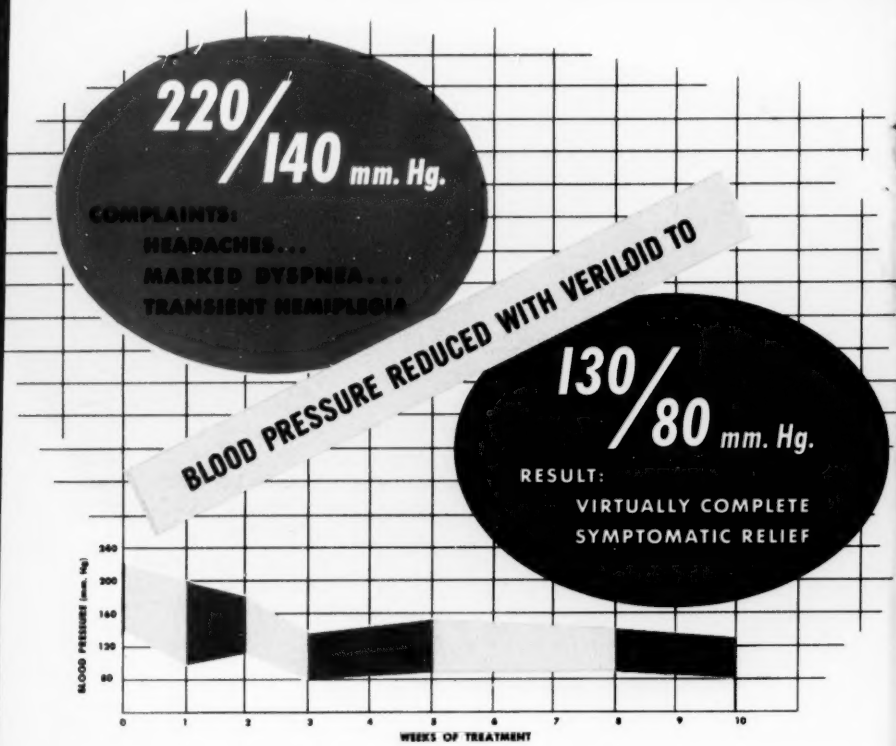

This excellent response to orally administered Veriloid was obtained in a male patient, aged 41.* Outpatient treatment with Veriloid for four months dropped his blood pressure to normal limits. Concurrently, he experienced considerable symptomatic improvement and was able to resume his former physically strenuous work. Special studies on this patient showed that the blood pressure was well controlled throughout the day.

Not every patient shows this spectacular response to oral Veriloid. However, a sufficiently large number do, warranting the administration of this hypotensive agent to every patient with elevation of blood pressure sufficient to require treatment. For this reason, the suggestion has been made that all hypertensive patients should be screened to identify those who respond well to veratrum preparations.**

*Kauntze, R., and Trounce, J.: Lancet *2*:1002 (Dec. 1) 1951.
**Page, I.H.: Pennsylvania M. J. *55*:737 (Aug.) 1952.

Veriloid is available in three dosage forms for oral administration:

Veriloid (plain) in 1, 2, and 3 mg. scored tablets; starting dosage 9 to 15 mg. daily, to be adjusted according to response and tolerance.

Veriloid with Phenobarbital (Veriloid-VP), each scored tablet presenting Veriloid 2 mg. and phenobarbital 15 mg.

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When you think of oral penicillin

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the most complete line of liquid oral penicillin

Whatever the indication or the patient's age, you will find a palatable Dramcillin product exactly suited to your needs. *White's* Dramcillin "family" assures:

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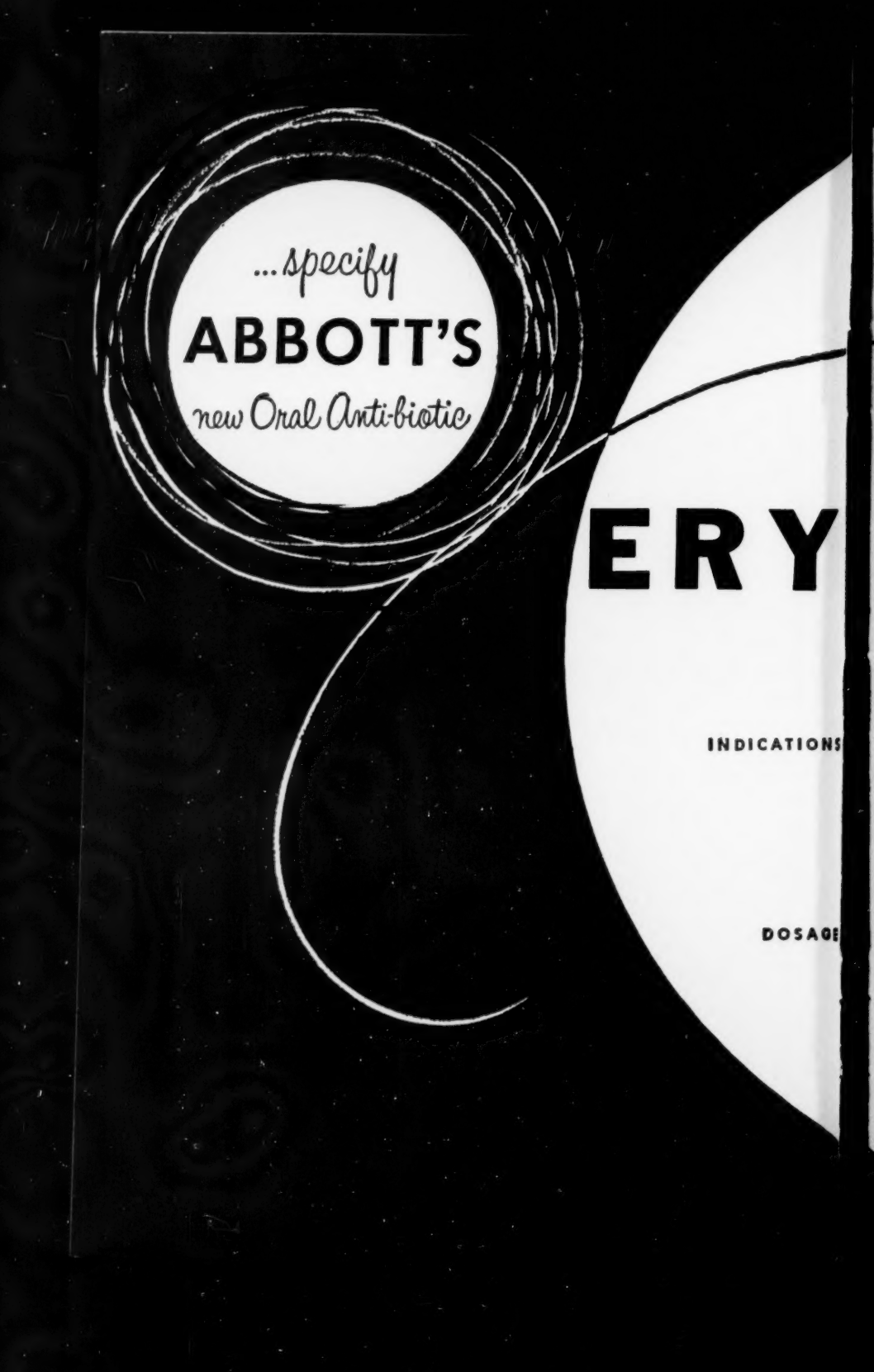
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E *specially effective against gram-positive organisms resistant to other antibiotics.*

L *ow toxicity; gastrointestinal disturbances rare; no serious side effects reported.*

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Pharyngitis, tonsillitis, scarlet fever, erysipelas, pneumococcic pneumonia, osteomyelitis, pyoderma. *Also other organisms* susceptible to its action, which include staphylococci, streptococci, pneumococci, *H. influenzae*, *H. pertussis*, and corynebacteria.

Total daily dose of 0.8 to 2 Gm., depending on severity of the infection. A total daily dose of 0.4 Gm. is often adequate in the treatment of pneumococcic pneumonia.

For the average adult an initial dose of 0.1 to 0.4 Gm. is followed by doses in the same range every four to six hours.

For severely ill patients doses up to 0.5 Gm. may be repeated at six-hour intervals if necessary. Satisfactory clinical response should appear in 24 to 48 hours if the causative organism is susceptible to ERYTHROCIN. Continue for 48 hours after temperature returns to normal.

Abbott

1. McGuire et al. (1952), J. Antibiotics & Chemo., 2:281, June. 2. Heilman et al. (1952), Proc. Staff Meet. Mayo Clin., 27:385, July 16. 3. Haight and Finland (1952), New Eng. J. Med., 247:227, Aug. 14.

In hypertension—

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Over 80 per cent of hypertensive patients can experience some benefit from Apresoline therapy if the following points are kept in mind:

1. The initial doses of Apresoline should be small (10 mg. after meals and at bedtime) and increased gradually over a period of weeks.

2. The dosage schedule should be adjusted to the individual response. It may take 8 weeks or more to realize optimal benefits.

3. Too much, too soon may lead to unnecessary side effects. Too little for too short a time may deny clinical benefits to some patients.

4. It is usually advisable to inform the patient that some secondary effects (e.g., headache) may occur at the start of therapy but that they almost always disappear as treatment is continued.

5. When secondary effects occur, they can often be managed by symptomatic treatment with antihistamines (e.g., Pyribenzamine,® tripelennamine Ciba), aspirin, barbiturates, etc.

Supplied: *Tablets*, 10 mg. (yellow, double-scored); 25 mg. (blue, coated); 50 mg. (pink, coated). Bottles of 100, 500 and 1000.

Ampuls, 1 cc. (20 mg. per cc.). Cartons of 5.

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RATIONAL— employs in each 5 cc. of aromatic syrup vehicle: glyceryl guaiacolate 100 mg. (unexcelled for increasing respiratory tract fluid), and desoxyephedrine 1 mg. (relieves bronchiolar constriction and improves patient's mood).

EFFECTIVE — stimulates maximum removal of sputum, with least frequent and least taxing cough.

PROVEN— as reported in clinical test: "[Robitussin] was significantly superior to the other preparations studied."*

*Cass, L. J. and Frederik, W. S.: Amer. Pract. and Dig. of Treat., 2:844, 1951. (In this study Robitussin was compared with ammonium chloride and terpin hydrate.)

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Forensic Medicine

ARTHUR L. H. STREET, LL.B.

Prepared especially for Modern Medicine

PROBLEM: A doctor who had previously discovered a cancerous condition in an exploratory operation testified that presumably an ovarian cyst had been ruptured in a fall, thereby hastening progress of the cancer from which the patient died. Was death by accident sufficiently proved for insurance purposes?

COURT'S ANSWER: No.

The Kansas Supreme Court applied the fundamental rule of law that a fact cannot be proved by presumption or inference based upon another presumption or inference (244 Pac. 2d 199).

PROBLEM: A hospital insurance certificate excluded benefits for treatment of preexisting physical conditions. Insured, who previously had two bunions, was hospitalized for treatment of one, which was injured accidentally. While operating the doctor included both bunions on the theory the uninjured one would ultimately need such treatment. Was insured entitled to hospital benefits under the certificate?

COURT'S ANSWER: Yes.

The Texas Court of Civil Appeals, Beaumont, reasoned: The condition treated was an injury sustained after the certificate was issued, even though the foot was more susceptible to injury because of the bunion.

Although no benefits were allowable for treatment of the uninjured bunion, no deduction was allowed on that account, because apparently the hospital expense would have been the same had treatment been given only to the injured bunion (252 S. W. 2d 507).

PROBLEM: In the trial of an automobile collision damage suit, the principal question was whether the impact, throwing plaintiff against the steering wheel of her car, caused a breast injury or whether a preexisting diseased condition accounted for most or all of the injury. Two doctors—the only medical experts testifying—ascribed the injury to the accident, although one of them had previously treated the woman for a breast ailment. But the opinions rested partly on the patient's statement that she was thrown violently against the wheel. Immediately after the accident she said that she was not hurt and she delayed three weeks in seeking treatment. Should a judgment in her favor for nominal damages only have been set aside for lack of medical testimony favoring a view that the accident did not contribute substantially to the breast condition?

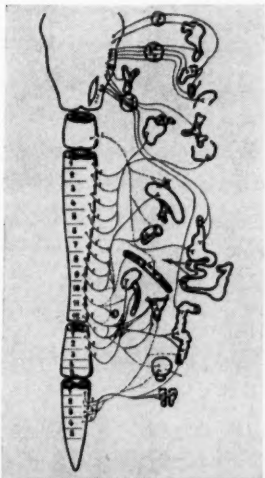
COURT'S ANSWER: No.

The California District Court of Appeal, Second District, Division 1, decided: Expert opinions are not necessarily binding upon juries, although not contradicted by other experts. They are to be weighed together with established facts, such as past medical history and admissions (249 Pac. 2d 846).

1

For this is the great error of our day in the treatment of the human body, that the physician separates the soul from the body.

PLATO *DIALOGUES, 380 B.C.*



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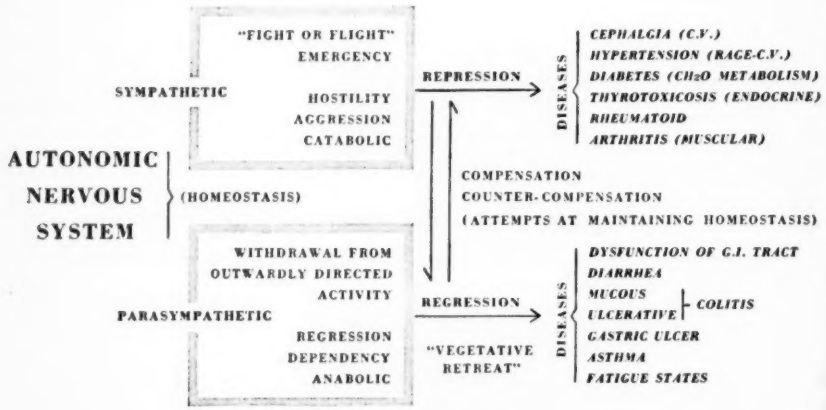
PSYCHOSOMATIC MEDICINE...

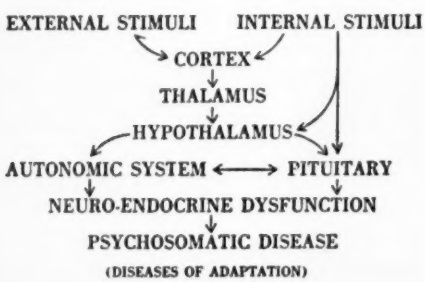
". . . a clinical field involving the study of abnormal functions set going by emotional stimulation of any system in the body and the study of lesions caused by abnormal functions."[1]



The above chart[2] summarizes the psychophysiologic responses of the autonomic nervous system whose normal function is to maintain homeostasis.

1. Cobb, S.: Borderlands of Psychiatry, (Monographs in Medicine and Public Health) Cambridge, Mass., Harvard Univ. Press, 1946, p.157. 2. Bradley, J. D.: North Carolina M. J. *12*:534 (Nov.) 1951.

The production of PSYCHOSOMATIC DISEASE



From this chart[2] it may be seen that external or internal stimuli or both might react via the cortex or lower centers upon the hypothalamus. This in turn stimulates the autonomic and pituitary adrenal system.

The place of Bellergal...

IN PSYCHOSOMATIC MEDICINE

It has been found that the use of BELLERGAL in conjunction with practical psychotherapy will offer complete relief in psychosomatic illness.

BELLERGAL is a product which contains a parasympathetic inhibitor, Bellafoline 0.1 mg. (1/600 gr.); a sympathetic inhibitor, ergotamine tartrate 0.3 mg. (1/210 gr.); and phenobarbital, a central sedative 20.0 mg. (⅓ gr.) — combined for inhibition of the transmission of noxious environmental stimuli.

"Rothlin first drew clear-cut conclusions from the newly recognized fact that disturbances in the vegetative nervous system almost invariably involve parasympathetic, as well as sympathetic, overstimulation. By means of animal experimentation he established the fact that the simultaneous administration of the vagus inhibitor Bellafoline (levorotatory alkaloids of belladonna leaves) and the sympathetic inhibitor Gynergen (ergotamine tartrate) does not diminish the specific effects of these two substances. Furthermore, he confirmed the pharmacological findings of Friedberg and Gordonoff, that the combination of the brainstem sedative phenobarbital with the two aforementioned drugs produces a preparation with distinctly enhanced central and peripheral effects."[3]

3. Wiltsie, J. W.: Chronic Intestinal Toxemia and Its Treatment, Baltimore, William Wood & Co., 1938, p. 242.

Clinical findings with Bellergal...

In The Climacteric...

Following a study of 125 women treated for climacteric symptoms, Kavinoky[4] concluded that,

"1. The vegetative nervous system plays an important role in the menopause syndrome.

2. Bellergal® is a safe and reliable sedative of the autonomic nervous system.

3. Bellergal® proved to be a useful adjunct in the treatment of 125 patients with various menopause disturbances."

4. Kavinoky, N. R.: J. Am. M. Women's A. 7:294 (Aug.) 1952.

IN ADJUNCTIVE THERAPY OF MIGRAINE

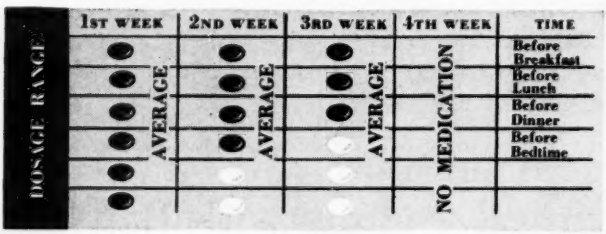
Von Witzleben[5] states, "The following is a summary of results obtained in my series of twenty-eight migraine (hemicrania) patients who received both psychotherapy and drug therapy [Bellergal]."

RESULTS	
Patients free of attacks for more than two years	15
Patients free of attacks for more than one year	7
Patients free of attacks for more than six months	4
Patients not improved	1
Patients relapse	1
Total	28

"... Bellergal will not replace or even act as a substitute for psychotherapy but if it is used judiciously in conjunction with suggestions and advice from clinicians, it will aid patients when regular contact with the psychiatrist is not possible. It has been observed to increase the length of time between attacks and it may even decrease the intensity of pain when hemicrania does occur."

5. Von Witzleben, H. D.: J. Missouri M. A. *49*:486 (June) 1952.

DOSAGE SCHEDULE



1. Adjust BELLERGAL® dosage as necessary to cope with severity of the condition.(averages given above).
2. Give medication one hour before meals and bedtime if possible.
3. Every fourth week should be medication-free to assess results of therapy.
4. Repeat course of treatment if symptoms recur.

Average dosage for adults: 3 or 4 tablets daily, usually 1 in the morning, 1 at noon, and 2 at bedtime.

SANDOZ Pharmaceuticals
Division of Sandoz Chemical Works, Inc. New York 14, New York

PROBLEM: After a maternity patient left a hospital, a sinus was discovered where an incision had been made in her perineum to prevent rupture in delivery. After defendant, an obstetrician, had unsuccessfully treated the sinus for several weeks by irrigation and curetting, another doctor excised the tract and performed a second operation, which disclosed a true fistula; the patient recovered rapidly. At the trial of the patient's suit for alleged malpractice, in not promptly providing the treatment required by her condition, the medical experts agreed that the circumstances justified the defendant's treatment as an effort to avoid surgery. There was no evidence that treatment was unduly delayed. The surgeon who operated testified that such sinus conditions "sometimes" heal under the treatment given by defendant. A jury found in plaintiff's favor. Did the trial judge properly set the verdict aside?

COURT'S ANSWER: Yes.

The Connecticut Supreme Court of Errors said that since no expert testimony was presented to show improper treatment, or prejudicial delay in administering it, the jury should not have been permitted to conjecture whether defendant was at fault (176 Atl. 123).

PROBLEM: The holder of a license to practice was duly notified of the time and place that application for revocation would be heard by the state medical board. She appeared by an attorney who requested continuance of the hearing on the ground of illness. No medical testimony was presented to establish her illness and a police surgeon testified that his examination the evening before indicated that she was able to attend the hearing. Did the board legally refuse to continue the hearing?

COURT'S ANSWER: Yes.

The Pennsylvania Superior Court noted a decision that advice of a physician will not excuse one from

(Continued on page 50)

in ARTHRITIS *and allied disorders*

BUTAZOLIDIN

rehabilitates the disabled patient

Through the use of BUTAZOLIDIN, many patients formerly bedridden, are now able to resume an active and useful life.

A totally new, synthetic compound, BUTAZOLIDIN (brand of phenylbutazone) is not related to the steroid hormones and its therapeutic effects are not dependent upon alteration of hormonal balance.

Clinically, BUTAZOLIDIN affords relief of pain, ranging from mild to complete, in approximately 75 per cent of cases. In the majority of instances, BUTAZOLIDIN also produces increased ease and range of motion through diminution of swelling and spasticity.

Characteristically effective in almost all forms of arthritis as well as in other painful musculoskeletal disorders, BUTAZOLIDIN affords the convenience of oral administration and the economy of relatively low cost.

Rheumatoid Arthritis[1-6]
Osteoarthritis[1,3,5]
Ankylosing Spondylitis[1,3-5]
Gout[1,4,5]
Psoriatic Arthritis[1,3,5]
Peritendinitis of the Shoulder[1,2,3,5]
Mixed Arthritis[1,5]
Bursitis[2]
Capsulitis[2]
Calcific Tendinitis[3]
Reflex dystrophy[3]
Menopausal arthralgia[3]
Lumbosacral strain[3]
Malum coxae senilis[5]
Still's disease[5]

Bibliography:
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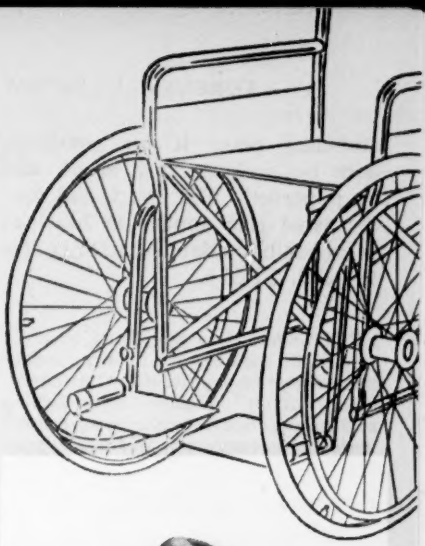

BUTAZOLIDIN has been reported to produce favorable results in all of the listed indications.

Treatment of the more transient conditions may be discontinued a few days after symptoms have been completely relieved. In the more chronic disorders BUTAZOLIDIN is usually continued indefinitely at the minimal effective dosage level required to avoid relapse. Frequently, the initial dosage of 600-800 mg. daily may be reduced to 400 mg. daily, or even less, without loss of effect.

In order to secure optimal results with minimal risk of side reactions physicians are urged to send for the brochure, "Essential Clinical Data on BUTAZOLIDIN," and other informative literature.

BUTAZOLIDIN® (brand of phenylbutazone) is available as coated tablets of 200 mg. and 100 mg.

attending court if his condition does not indicate that health will be imperiled. The court said that the same rule applies to hearings before public administrative bodies (94 Atl. 2d 61).

PROBLEM: Did any court ever decide that a member of a medical society was subject to expulsion for "dishonorable conduct" because after having sold his practice he broke an agreement with his successor not to resume practice?

COURT'S ANSWER: Yes.

The Massachusetts Supreme Judicial Court so decided in 1853 (12 Cushing's Reports, 402).

The Massachusetts Medical Society was upheld in expelling Dr. B on recommendation of a committee. The committee reported that had any consideration been mentioned in Dr. B's agreement to relinquish his practice, "this would more properly be a subject of legal investigation than one of this kind; but, as it is, they are of the opinion that, *in moral point of view*, respondent is guilty of the charge."

Ground for expulsion having been thus established, no decision was apparently reached on an additional charge that Dr. B had manufactured, vended, and recommended a certain nostrum called "Watona." He admitted that, but denied amenability to the Society, on the ground that at that time he

(Continued on page 54)

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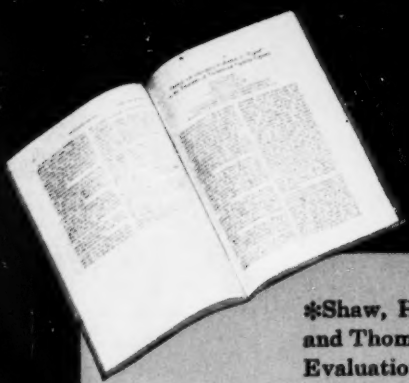
in Every Age Group

The 100 patients in a carefully controlled evaluation of Vagisol in trichomoniasis ranged from 10 years to 80 years in age. Culture-established cure was shown in 98 of these patients, including every age group.



*Shaw, H. N.; Henriksen, E.; Kessel, J. F., and Thompson, C. F.: Clinical and Laboratory Evaluation of "Vagisol" in the Treatment of Trichomonas Vaginalis Vaginitis, Western J. of Surg., Obst. & Gynec. *60*:563 (Nov.) 1952.

In Trichomonas Vaginitis

Two important advantages of Vagisol in trichomonas vaginitis were established in the study cited:

Remarkably rapid relief from the distressing symptoms: pruritus, burning, suprapubic pain, dyspareunia, dysuria. The patients were symptom-free in 2.15 mean patient days. The controls, treated with another trichomonacide, required 6.75 days.

A 98% cure rate, in ⅓ to ⅕ the time required by the control group. Vagisol produced culture-demonstrable cures for 72% of the patients in 18 days, for 22% in 36 days, and for 4% in 54 days. Of the controls, 25% required 56 days of therapy, 42.5% 84 days, and 20% required 112 days.

Vagisol proved equally effective in every age group—in childhood, during the reproductive years, and after the menopause.

Though quickly relieved of their discomfort, patients cooperated and remained on Vagisol therapy.

Vagisol Suppositabs, supplied in bottles of 36, are odorless and nonstaining. Each Suppositab contains:

Phenylmercuric Acetate	3.0 mg.
Tyrothricin	0.5 mg.
Succinic Acid	12.5 mg.
Papain	25.0 mg.
Sodium Lauryl Sulfate	3.0 mg.
Lactose	0.75 Gm.

Vagisol is available on prescription through any pharmacy. For detailed literature, clinical test samples, and patient instruction leaflets, physicians are invited to write to Smith-Dorsey, Lincoln, Nebraska (a Division of The Wander Company).

VAGISOL

A DORSEY PREPARATION

acted as a druggist and not as a medical practitioner. The prosecutor of the charges countered that recommendation of the nostrum fell within practice of medicine.

PROBLEM: In an automobile accident case, the defendant claimed that an ailment, which the plaintiff attributed to the accident, had previously existed. Under Florida law, did the trial judge properly require a doctor who had previously treated the plaintiff to testify whether the ailment then existed?

COURT'S ANSWER: Yes.

The Florida Supreme Court decided that a statute adopted in 1951, forbidding furnishing of doctors' "reports" on medical examinations to other parties without the patient's consent, did not apply to the case nor modify the preexisting common-law rule in force in Florida, under which communications by patient to physician are not privileged from disclosure in court.

The opinion of the court is of general interest because it incidentally dealt with a contention that, apart from statutes, the Hippocratic oath seals the doctor's mouth. The court referred to that part of the oath which binds the doctor to "keep secret" knowledge "in the exercise of my profession or outside of my profession or in the daily commerce with men, which ought not to be spread abroad." Deciding that the oath

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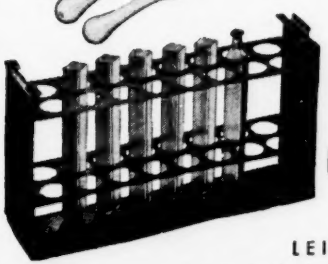

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does not justify refusal by a doctor to disclose in court information pertinent to litigation, the court observed that the oath is not confined to secrets arising from professional services, that it merely forbids "unseemly circulation" of secrets, and that the doctor cannot determine for himself "whether he should divulge it and whether telling it at the command of the court would amount to spreading it abroad" (62 So. 2d 1953).

PROBLEM: Under Kentucky laws, right to sue for malpractice expires unless suit is brought within one year, but time during which defendant "obstructs the prosecution" of the suit is not counted as part of the year. Allegedly, a doctor, in treating pneumonia in 1929, left a rubber tube 6 in. long in the patient's lung. After ten days the patient threatened to sue unless the doctor removed the tube. Relying on the doctor's assurance that the tube would do no harm and would be absorbed, the patient did not sue until February 1949, about eight months after pulmonary hemorrhage disclosed that the tube had not been absorbed. Assuming these facts to be true, was the suit subject to dismissal as not having been brought in time?

COURT'S ANSWER: No.

The Kentucky Court of Appeals reasoned: The courts generally declare that time for suing is extended when the physician conceals facts showing liability until the patient discovers, or ought to discover, those facts. Although ordinarily the concealment must be affirmative, in some cases mere silence may amount to fraudulent concealment—when the circumstances require disclosure. A doctor must use utmost good faith and truthfulness, "at the peril of being held liable for damages for fraud and deceit" (249 S. W. 2d 791).

For the patient whose feet are "always cold"—

For patients with impaired peripheral circulation, RONIACOL® ELIXIR 'Roche' provides a well-tolerated vasodilator in tasty, convenient form. Also available in tablets, Roniacol (beta-pyridyl-carbinol) is especially useful for prolonged therapy.

Roniacol 'Roche' — a well-tolerated vasodilator —

Roniacol usually provides effective vasodilation without likelihood of severe flushes or other side reactions. For peripheral vascular disorders and for maintenance therapy in angina pectoris.

Washington LETTER

How New Cabinet Post Will Affect Physicians

WILL the new Department of Health, Education and Welfare make any real difference to the average practitioner? The answer definitely is yes, although the changes will be gradual and some doctors will be affected more than others.

This is evident from a study of the new department's administrative structure and from the commitments made by Secretary Hobby and other administration leaders who will be in charge for at least four years.

"That's his wife. She watches over him like a hawk."

At first there will be no difference at all. The department is so cumbersome and medical programs so widely scattered through its various operations that abrupt, overnight alterations would be impossible, even if advisable. Furthermore, Secretary Hobby and her various hand-picked subordinates will need weeks if not months to make the full department responsive to new policies. Once that stage is reached, the doctors of the country may look for improvements.

Then a "recognized leader in the medical field with wide nongovernmental experience" will be constantly at the Secretary's side, passing on to her the doctors' points of view on new legislation, new regulations, and every other departmental activity with a medical interest. The expectation is that the viewpoint of the doctors will be given more consideration than heretofore in preparation of the regulations.

To insure adequate representation in the right place for the medical profession, the new department has a special position not found in other cabinet departments. It is titled Special Assistant to the Secretary for Health and

Medical Affairs. This official has to be selected from among recognized leaders in the medical field with wide nongovernmental experience and, presumably, would be a physician, although this isn't a legal requirement.

The law states that this medical assistant shall review all medical developments within the department and make recommendations to the Secretary on all medical or health legislation regardless of what department or agency is affected. On this the law (Reorganization Plan No. 1 of 1953) states that he "shall review the health and medical programs of the department and advise the Secretary with respect to the improvement of such programs and with respect to necessary legislation in the health and medical fields."

This means that any new development in U. S. Public Health Service will be subject to the screening of the medical assistant, as will any proposal or regulations of a medical nature arising in the other five offices—Office of Education, Social Security Administration, the Field Service, Office of Vocational Rehabilitation, and Food and Drug Administration.

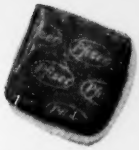
A few specific examples:

• The new medical assistant will be able to express his views to the Secretary on suggestions for amending the prescription law.

(Continued on page 64)

new!

Candettes



double antibiotic action

Combined action of bacitracin and polymyxin, topically effective against mixed bacterial flora of mouth and throat.

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Antibiotic

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Bacitracin-Polymyxin B Troches

non-sensitizing

Virtually non-sensitizing, bacitracin and polymyxin may be used topically without significant local reaction — or sensitizing the patient against systemic therapy. Bacterial resistance is minimal.

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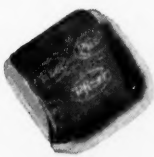
and fresh orange flavored

a pleasant, candy-like troche to encourage patient acceptance.



Candettes antibiotic troches
polymyxin B 1,000 units (0.1 mg.)
bacitracin 50 units

*TRADEMARK, CHAS. PFIZER & CO., INC.

Pfizer *World's Largest Producer of Antibiotics*

Antibiotic Division, Chas. Pfizer & Co., Inc., Brooklyn 6, N.Y.

CONSTIPATION*

possibly the

greatest single medical problem

of the patient who is over **40**

In these cases, laxation *alone* isn't enough.

Because constipation in this age group is usually associated with indigestion and biliary stasis.

Prescribe Caroid[R] and Bile Salts with Phenolphthalein to obtain these three beneficial actions:

cholerotic action — for an increased flow of bile

digestant action — aids protein and fat digestion

laxative action — gentle laxation with minimal dosage

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write for professional samples to

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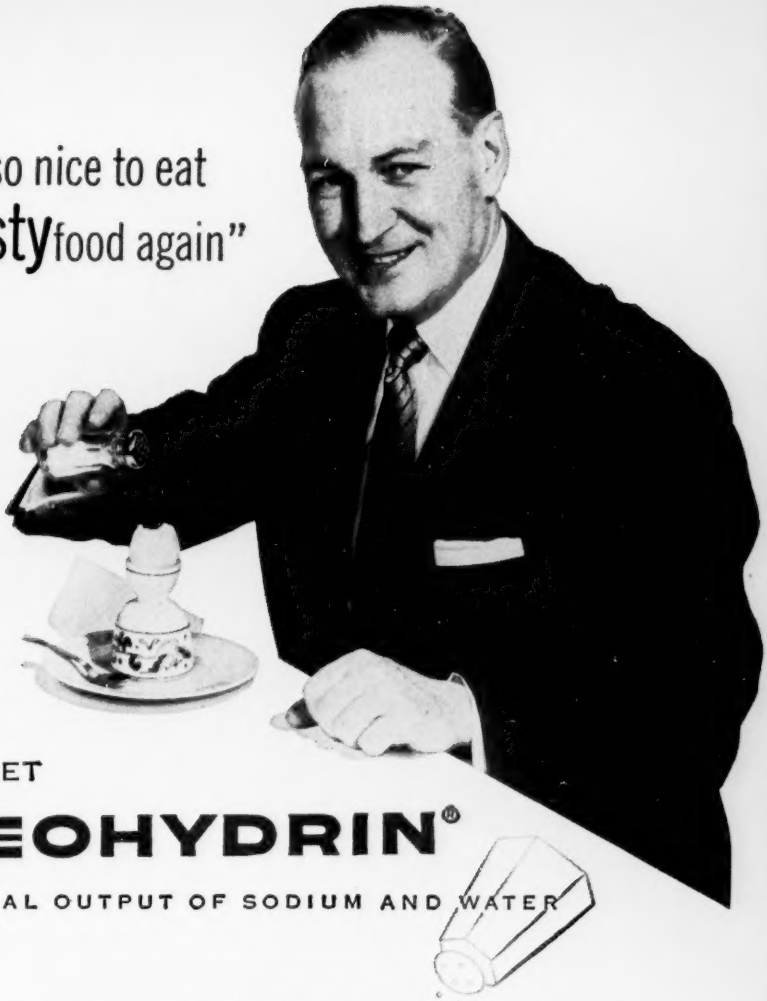
*Rehfuss, M. E., Indigestion, Philadelphia, W. B. Saunders Co., 1943, p. 322

CAROID AND BILE SALTS *tablets*

Specifically indicated in ***biliary dyspepsia and constipation***



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"...our results...striking... dramatic..."[1]

"...rapid..."[1,2]

"...never (were) other iron salts so efficacious in pregnant patients."[1]

"...more active than the unmodified iron salt (ferrous sulfate)"[2]

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During the past six years Mol-Iron has repeatedly been demonstrated[1-12] to provide the most effective oral iron therapy known. In a recent unique diagnostic and therapeutic study, utilizing newer biochemical determinations in addition to standard hematologic studies, the author[8] described the effect of Mol-Iron as " . . . the equivalent of a 350 cc. blood transfusion . . . in the severely anemic patient . . . Six weeks of . . . (Mol-Iron) therapy will in the anemic mother produce the equivalent of 4 transfusions at a fraction (1/40) of the cost."

As for tolerance: "Of the 75 patients receiving (Mol-Iron) . . . , (only) one was forced to stop treatment because of gastrointestinal disturbances."

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MOL-IRON Tablets—for older children and adults.

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1. Dieckmann, W. J. and Priddle, H. D.: Am. J. Obstet. & Gynec. 57:541, 1949.
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12. Briscoe, C. C.: Am. J. Obstet. & Gynec. 63:99. 1952.

- He will advise her on regulations or new programs of rehabilitation.
- He will screen any suggestions of a health or medical nature coming from the Office of Education.
- If Congress enacts legislation for Social Security payments to persons found to be totally and permanently disabled, the medical assistant would have an important role in setting up criteria for determination of disability. In the last few years this particular issue has repeatedly aroused the American Medical Association.
- The medical assistant also would evaluate any medical legislation affecting the general public, even if the department as such would not be involved in administration.

At the time the new department was proposed, Mrs. Hobby not only reaffirmed her intention to assign to this assistant all the responsibilities set forth in the law, but also defined other responsibilities to be delegated to him.

He will represent her in all dealings with such professional groups as the American Medical Association, American Hospital Association, and American Dental Association. Furthermore, he will perform the same function regarding World Health Organization and other international bodies.

In addition to providing for the medical assistant, the new department differs from others in a second important respect. The Secretary may, at her discretion, delegate to the medical assistant the authority to perform any of the functions of the Secretary. The wording of the law on this: "The Secretary may from time to time make such provisions as the Secretary deems

(Continued on page 70)

"Bemotinic" Liquid

in the common anemias

Unequalled for taste
Unusually palatable. No need to dilute or mask . . . just a pleasantly rich orange flavor, with no aftertaste.

Effective action
Provides essential factors for maximal hemopoietic and clinical response . . . includes a B_{12} potentiator.

Simple administration
Directly from the spoon because of high degree of palatability . . . smooth, nonviscous, easy-pouring.

Each teaspoonful (5 cc.) contains:

Ferric ammonium citrate	200.0 mg.
Vitamin B_{12} U.S.P. (crystalline)	4.0 mcg.
Extractive as obtained from 450.0 mg. of fresh gastric tissue	
Folic acid	0.33 mg.
Thiamine HCl (B_1)	1.5 mg.
Riboflavin (B_2)	1.0 mg.
Pyridoxine HCl (B_6)	0.2 mg.

Suggested dosage:
Adults: 1 to 2 teaspoonfuls
Children: ½ to 1 teaspoonful
Three times daily, or more as required.
No. 940 — Supplied in bottles of 16 fluidounces and 1 gallon.

Also Available

"BEMOTINIC"® CAPSULES

No. 340 — Bottles of 100 and 1,000.

Each capsule contains:

Ferrous sulfate exsic. (3 gr.)	200.0 mg.
Vitamin B_{12} U.S.P. (crystalline)	10.0 mcg.
Gastric mucosa (dried)	100.0 mg.
Desiccated liver substance, N.F.	100.0 mg.
Folic acid	0.67 mg.
Thiamine HCl (B_1)	10.0 mg.
Vitamin C ascorbic acid)	50.0 mg.

Suggested dosage: 1 or 2 capsules three times daily, or as directed by the physician. Preferably taken with food.

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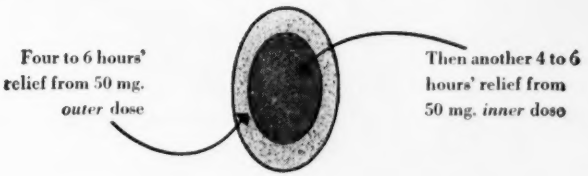

less frequent dosage
uninterrupted night rest
greater freedom from side effects

PRANTAL*
3 forms for more flexible therapy

PRANTAL Repeat Action Tablets, 100 mg.
Dosage: One or two tablets every eight hours.

PRANTAL Tablets (plain), 100 mg., scored.
Dosage: One or two tablets every six hours.

PRANTAL Injection (subcutaneous or intramuscular), 25 mg. per cc., 10 cc. vials.
Dosage: 0.5 mg. per Kg. of body weight every six hours.

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I'M SO CROSS AND TIRED,"

is the constant complaint of the obese patient on a restricted diet when nutritional support is neglected.

AMPLUS combats depression and irritability by providing the "mood-elevating effect" of dextro-Amphetamine Sulfate and the Vitamin-Mineral support so essential whenever food intake is restricted.

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Calcium	242 mg.
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Copper	1 mg.
Iodine	0.15 mg.
Iron	3.33 mg.
Manganese	0.33 mg.
Molybdenum	0.2 mg.
Magnesium	2 mg.
Phosphorus	187 mg.
Potassium	1.7 mg.
Zinc	0.4 mg.
Vitamin A	5,000 U.S.P. Units
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Thiamine Hydrochloride	2 mg.
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appropriate authorizing the performance of any of the functions of the Secretary by any other officer, or by any agency or employee, of the Department."

When all of these functions are added up, the question appears not to be whether this medical assistant has too little responsibility, but whether under a sympathetic Secretary he won't have more than he can discharge.

Washington Notes

¶ Under the preliminary allocation plans worked out by the Office of Defense Mobilization, part of the gamma globulin supply for poliomyelitis cases will be distributed to states, the remainder kept in a national pool for use in epidemic areas.

¶ The annual report of the Office of Vocational Rehabilitation again confirms that federal dollars spent in rehabilitation are more than paid back within three years in income taxes by rehabilitated persons.

¶ The House Interstate and Foreign Commerce Committee appears to be looking with sympathy if not enthusiasm on Rep. Frances P. Bolton's bill for federal aid to nursing schools. Because a part of the proposal is "open end," there is no way to estimate just what the program would cost.

¶ In endorsing the new Department of Health, Education and Welfare, the American Medical Association's House of Delegates specifically reserved the right to criticize the department in the future if it doesn't operate as it should. Incidentally, the Association's policy of advocating the eventual establishment of a separate Department of

a standard measure

to avert or allay allergic distress...

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BENADRYL Hydrochloride is available in a variety of forms—including Kapseals,® 50 mg. each; Capsules, 25 mg. each; Elixir, 10 mg. per teaspoonful; and Steri-Vials,® 10 mg. per cc. for parenteral therapy.

MEDICAMENTA VERA

Parke, Davis & Company

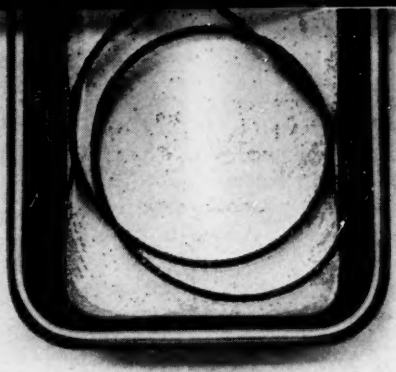
DETROIT, MICHIGAN

Health has not been compromised; this will be pushed in the future as opportunity permits.

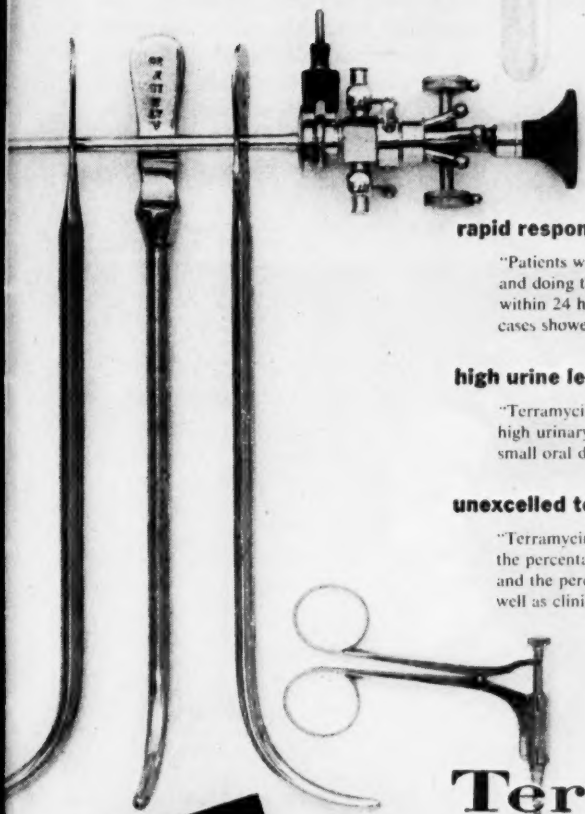
¶ Contrary to some observers, the Supreme Court decision in the Dr. Stanley Orloff case did not affirm the constitutionality of the Doctor Draft law as such. The issues in this case did not represent a frontal attack on the law. Consequently, other suits may be expected in the future until a firm decision comes from the Court.

¶ Meanwhile, at this writing the Defense Department's bill for extending and amending the Doctor Draft law has not been introduced; the best information is that the proposal is not faring too well in other government agencies that have the privilege of reviewing it, particularly Selective Service and Office of Defense Mobilization. With Defense Secretary Wilson advising a

"Temperature normal, pulse 76, blood pressure 140 . . . and you?"



IN URINARY TRACT INFECTIONS



rapid response

"Patients with pyelitis were well and doing their usual duties within 24 hours . . ."[1] ". . . resistant cases showed remarkable response."[2]

high urine levels

"Terramycin was selected . . . in view of high urinary excretion rate following small oral doses of the antibiotic."[1]

unexcelled toleration

"Terramycin is generally well tolerated, the percentage of relapses being low and the percentage of bacteriological as well as clinical cures high."[3]

1. Canad. M. A. J. 66:151 (Feb.) 1952.
2. J. Urol. 67:762 (May) 1952.
3. Ibid. 69:315 (Feb.) 1953.

Terramycin

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Pfizer

read Pfizer Spectrum weekly in the J.A.M.A.

cutdown on drafted manpower, there may not be so much need for drafted doctors. An administrative change at Defense Department should give more weight to civilian opinion on military medical matters, including the number of men to be called up monthly in the Doctor Draft. The Armed Forces Medical Policy Council is abolished and a one man office set up in its place. Dr. Melvin Casberg, who headed the Council, is filling the new post, as Assistant to the Secretary. He will report directly to Secretary Wilson, but the Manpower Secretary may make separate recommendations to Mr. Wilson.

¶ Opposition to fluoridation of water supplies for prevention of dental caries continues. Rep. Roy Weir (D., Minn.) has introduced a bill to forbid any government—federal, state, county, city—to fluoridate water.

¶ A bill by Rep. Cleveland M. Bailey (D., W. Va.) proposes that the federal government initiate a pilot plan for clinics for narcotic addicts and alcoholics. It would be handled through a Federal Bureau of Clinics, which would simply take over the Public Health Service narcotic hospitals, add treatment of alcoholics, and gradually open more clinics and hospitals. This has some chance for success this session because it would not involve much additional money and would have public appeal.

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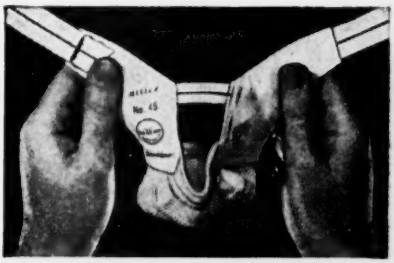
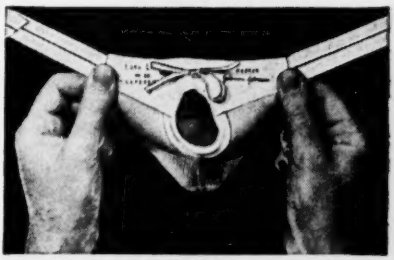
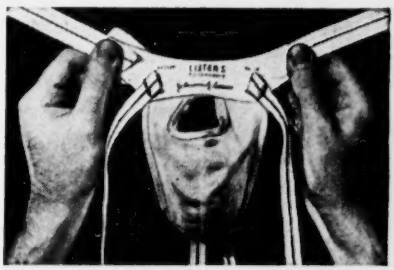


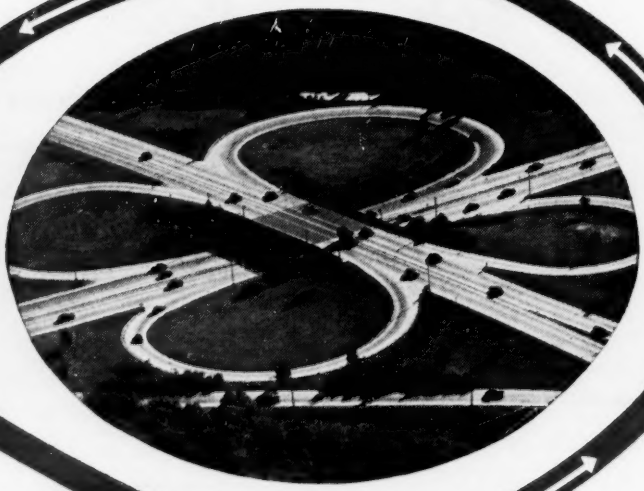
J. P. 45 Without legstraps. Many slender men prefer its freedom. Elastic strip in yoke is self-adjusting. Large, Medium, Small.....75c



No. 101 Without legstraps. Drawstring in yoke can be adjusted. Knitted pouch is suspended from sides, for upward lift. L.M.S.....$1.00



Lister's No. 10 Legstraps offer greater immobilization. Felt pad under waistband buckle and chamois pad in crotch. L.M.S.....$1.25 Also available, Lister's No. 4 leg type, $1.00; and the de luxe Diamond J, $1.50.



free flow

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MODERN MEDICINE
THE JOURNAL OF DIAGNOSIS AND TREATMENT

Diagnosis of Angina Pectoris

the Master two-step test

A Modern Medicine Editorial

For years I have been seeing patients with typical stories of angina pectoris and normal electrocardiograms, and for years I have followed the practice of telling these men that they almost certainly have narrowed coronary arteries and hence will have to go easy. For years I have seen these patients go from one physician to another getting more and more confused and upset with every conflicting opinion received.

For years, also, while trying to reassure cardiac hypochondriacs, I have often been blocked by having the man say, "Yes, I know I have a normal electrocardiogram, but a half dozen of my friends who received that report dropped dead shortly afterward."

For the last few years I have been using the Master two-step test in which the patient with a normal electrocardiogram is made to go up and down two 9-in. steps a certain number of times, depending on his age, weight, and sex. After this exercise, in cases of angina pectoris, the electrocardiogram usually shows certain changes, notably a definite depression of the RS-T segment, which clear away after a few minutes' rest. If no change is noted with the first period of exercise, a second test, made right away, has a 30% chance of showing the abnormality, granting that the person has a narrowed coronary artery.

I agree with Master's statement that practically always, if a man has a typical story of angina on effort, the two-step test, single or double, will confirm the clinical diagnosis. In my hands the test has been very helpful in settling the doubts of

puzzled patients, and its prognostic value has been excellent. In a few instances in which the patient has been positively reassured by several cardiologists, who evidently put all their trust in negative electrocardiograms, my statement for the examination has been paid several months later by the administrator of the man's estate!

WALTER C. ALVAREZ

Pheochromocytomas

Every so often we physicians get much concerned over some discovery. For months we read about it in every other issue of our medical journals, and we get to worrying because we do not see any cases. Perhaps in our anxiety to keep modern and up to date we start diagnosing the disease on the basis of insufficient evidence, assuming that we are being keen enough to recognize *formes frustes.*

A good example of this was the fad a few years ago of diagnosing hyperinsulinism in hundreds of cases in which an overly nervous woman cured her slight dizziness or bit of midmorning or midafternoon fatigue by a fifteen-minute session in the company cafeteria, or at the soda fountain, with a cup of black coffee and a cigaret!

These remarks are occasioned by my noticing in a recent article that so far, at the Mayo Clinic, with its 140,000 cases a year, the clinicians have found and removed just 25 pheochromocytomas! That should now somewhat relieve the minds of those of us who, in the next ten years, with our average-sized practices, will not see a single case.—W.C.A.

A Great Timesaver

So many physicians wrote in to express interest in my editorial on the need for physicians' trying to save time that I here add a note on my own greatest time-saver—a dictating machine.

For years I have used one of these machines to take down histories. Instead of writing I keep putting into the machine, sentence by sentence, an abstract of what the patient said. Practically never does a patient object to this. In this way I can take and record a long detailed history in a few minutes.—W.C.A.

Fertility and Sterility Symposium

Foreword

ABNER I. WEISMAN, M.D.
New York City

THE subject of fertility and sterility has recently grown to great proportions and is engaging the interest of physicians in many parts of the world. This interest is reflected in the following Symposium. Contributions have been sought from outstanding authorities. Results of their extensive research on the various aspects of human fertility are here made available to the general medical profession.

This Symposium is selective rather than comprehensive. It represents but a sampling of the large body of information that will be brought out in the forthcoming First World Congress on Fertility and Sterility to be held in New York City from May 25 to 31, 1953, at which scientists from all over the world will gather and contribute their share of new research in the field of human reproduction.

Meanwhile we believe the Symposium published here will serve to stimulate the interest of doctors generally in finding ways of helping relatively infertile couples to have babies of their own, as well as providing a considerable amount of knowledge as to how this can be accomplished.

I should like to take this opportunity to thank the contributing physicians for their cooperation in making the information contained in this Symposium available to the general medical profession.

*Associate Secretary-General, International Fertility Association; Managing Editor, *Fertility and Sterility*.

CLINICAL SYMPOSIUM

Fertility and Sterility

Part I—Male Aspects

*Semen Examination
*Testicular Biopsy
*Evaluation of General Therapy
*Vasoepididymal Duct Obstruction

Papers in this symposium were prepared exclusively for Modern Medicine. The Symposium was outlined and edited by Abner I. Weisman, M.D.

Prepared for Modern Medicine

Significance of the Semen Examination

WALTER W. WILLIAMS, M.D.*
Springfield Hospital, Springfield, Mass.

IN the study of an infertile couple, one of the first diagnostic tests to be performed is a semen analysis. This procedure alone will often reveal the etiology of marital sterility. The laboratory examination of fresh semen will usually serve to identify the highly fertile and the hopelessly sterile males.

The health of the germ plasm is mirrored in the condition of the spermatozoa. In a large sperm population many cells may be abnormal in one respect or another without materially interfering with fertility, but the point of tolerance for pathologic spermatozoa is often exceeded. This results in varying degrees of infertility according to the extent and permanency of the disorder.

It should be borne in mind that the fertilizing ability of a sperm population may be lost because of low vitality without obvious micropathology. Therefore, the clinical status of the patient should always be considered in conjunction with the laboratory findings. Such factors as a low basal metabolic rate, anemia, sexual overindulgence, and various somatic disturbances will sometimes provide a more secure basis for prognosis than the seminal findings alone.

The more normal semen specimen can usually be distinguished by the exceptionally large concentration of highly motile cells migrating rapidly in a clear microscopic field free from other formed elements, whereas abnormal semen is characterized by reduced motility, a paucity of cells, and the presence of abnormally formed cells, detritus, and, often, crystals.

As a precursor of the spermatic picture, there may be [1] a germ plasm aplasia, which is shown by the absence of spermatozoa in the ejaculate, to be differentiated from a vasoepididymal obstruction by means of testicular biopsy, [2] a germinal hypoplasia as indicated by paucity or absence of ejaculated spermatozoa, [3] asthenospermia, which is recognized by subnormal motility and early death of the spermatozoa, or [4] a germinal dysplasia, indicated by an excessively high ratio of structurally imperfect spermatozoa.

Dysplastic germinal tissue is very commonly hypoplastic, and this results in hypospermatogenesis. A germinal dysplasia which is associated with a paucity of spermatozoa gives the poorest prognosis but, if only a few normal cells are present, conception occasionally occurs. An oligospermia associated with a relatively normal sperm picture offers a much better prognosis.

*Geneticist, Springfield Hospital, Springfield, Mass.

The following tabulation shows the incidence of seminal factors in 927 infertile couples studied by the writer:

Essentially normal	47%
Severe spermatic dysplasia—over 40% abnormal	26%
Asthenospermia only—less than 50% motile	10.7%
Oligospermia only—less than 40,000,000 per cubic centimeter	9.2%
Azoospermia	7.1%

Male infertility is usually caused by a fundamental disorder of the germ plasm, apparently of embryonal origin. About 75% of azoospermic cases are so caused, and these are frequently associated with hypoplastic testes. In my own series, epididymal obstruction from neisserian infection accounts for less than 2% of the total infertility.

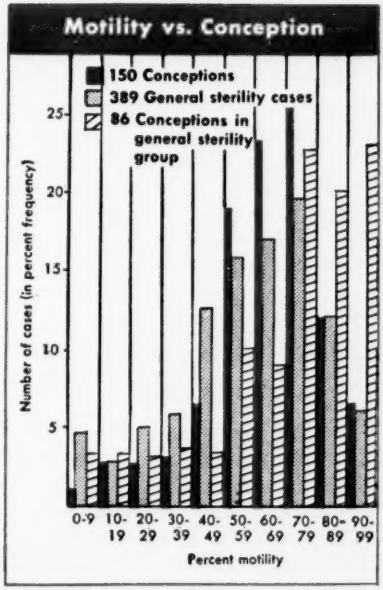
The fertilizing power of spermatozoa depends upon two main factors: [1] adequate vitality to insure migration, survival, and union with the ovum, and [2] structural suitability for such union. Various unsuccessful attempts have been made to fix precise standards for normal semen so that the fertile specimens may be more clearly distinguished from the infertile. However, when studying cases clinically, we find no clear-cut line of demarcation between fertile and infertile semen specimens by which we can predict precisely which are capable of causing conception.

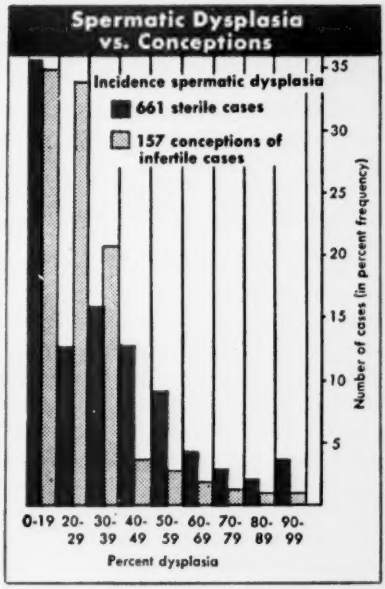
Experience has shown that many men who produce highly abnormal semen will prove to be fertile. In general, however, semen specimens represent different grades of pathology and result accordingly in different degrees of fertility. The potential fertility depends upon the extent to which the sperm population has been injured, and whether the injury is of a permanent or transitory character.

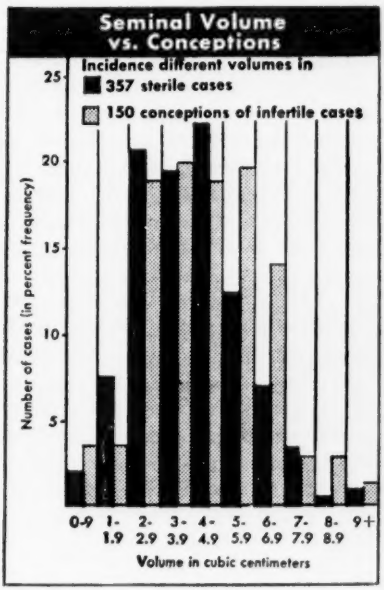
In Graph 1, it will be seen that the ratio of conceptions is very low when spermatic motility is less than 40%. A generally low grade of motility involving the entire sperm population is also highly significant. An especially low ratio of conceptions is noted in groups with more than 40% morphologically abnormal spermatozoa in the semen (Graph 2). It is evident that populations falling into the higher motility and normal morphology brackets result in a much greater potential fertility than those with poor motility or a high ratio of pathologic cells.

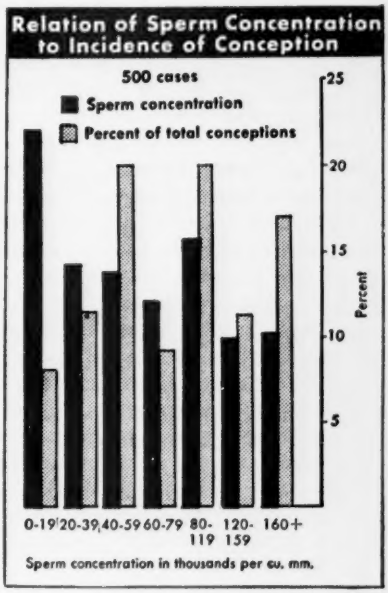
The relationship of seminal volume and sperm concentration to fertility has been somewhat overemphasized. Testicular hypoplasia is often associated with reduced function of the accessory genital glands, which causes a reduction of seminal volume, but, for the most part, the range of volume for the fertile and the infertile groups is quite similar. Except for extreme cases with less than 1.5 cc. or more than 7 cc., the volume seems to provide absolutely no index to the state of fertility (Graph 3).

It will be observed in Graph 4 that the ratio of conceptions is not materially influenced by the sperm concentration. The spermatozoa were of poor quality in a large


Motility vs. Conception
150 Conceptions
389 General sterility cases
86 Conceptions in general sterility group
Number of cases (in percent frequency)
0-9 10-19 20-29 30-39 40-49 50-59 60-69 70-79 80-89 90-99
Percent motility


Spermatic Dysplasia vs. Conceptions
Incidence spermatic dysplasia
661 sterile cases
157 conceptions of infertile cases
Number of cases (in percent frequency)
0-19 20-29 30-39 40-49 50-59 60-69 70-79 80-89 90-99
Percent dysplasia


Seminal Volume vs. Conceptions
Incidence different volumes in
357 sterile cases
150 conceptions of infertile cases
Number of cases (in percent frequency)
0-9 1-1.9 2-2.9 3-3.9 4-4.9 5-5.9 6-6.9 7-7.9 8-8.9 9+
Volume in cubic centimeters


Relation of Sperm Concentration to Incidence of Conception
500 cases
Sperm concentration
Percent of total conceptions
Percent
0-19 20-39 40-59 60-79 80-119 120-159 160+
Sperm concentration in thousands per cu. mm.

proportion of the sperm concentrations of less than 40,000,000 per cubic centimeter. These caused relatively few conceptions, but the presence of a number of cases with high quality cells but low sperm concentration served to raise the conception rate of the group as a whole.

A few conceptions occurred with sperm concentrations of less than 1,000,000 per cubic centimeter. There was a higher ratio of more normal populations in cases with sperm concentrations of over 40,000,000 per cubic centimeter, but with these healthier patients, the ratio of conceptions was markedly reduced by adverse factors in the wife, particularly faulty ovulation and tubal disease.

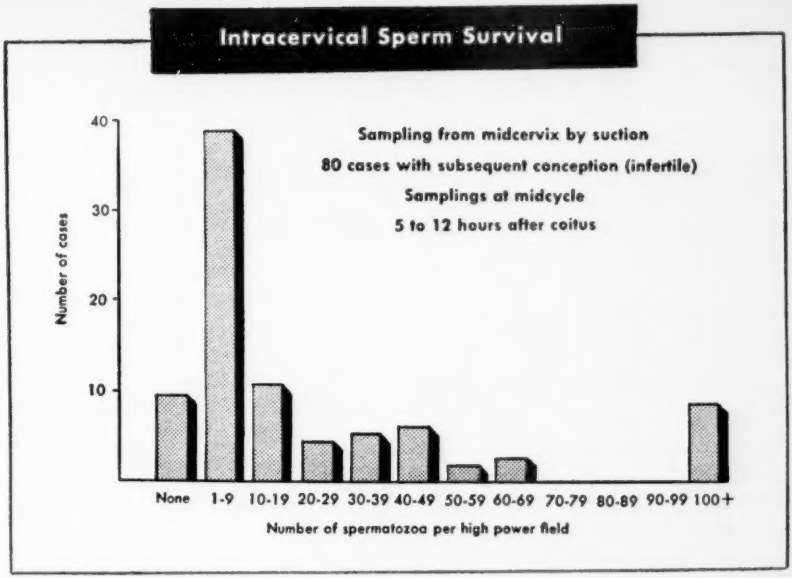
That the rate of conception is not seriously impaired by rather low sperm concentrations of healthy spermatozoa is suggested not only by the numerous conceptions occurring from subjects with low sperm concentrations, but also by the observation that a small fraction of a highly normal ejaculate can be used successfully for artificial insemination in both man and animals.

Postcoital examinations are so commonly employed to test the fertilizing ability of sperm populations that it is well to consider their clinical significance. Graph 5 shows that it is the exception rather than the rule that large numbers of live spermatozoa are obtained from the cervical mucus in the relatively infertile cases in which conception occurs. In some cases, the sperm migration and survival are so limited that no spermatozoa at all are found at this site.

This indicates that the cervical canal, and especially the region of the internal ring, imposes a considerable barrier to sperm migration, so that only a few of the more healthy cells find their way through. On the other hand, in many infertile cases, extremely high concentrations of spermatozoa are found in the cervical mucus. The postcoital examination, therefore, is of doubtful value as a sole criterion of male fertility.

Since testicular biopsies have been extensively recommended for evaluating male fertility, it may be well to compare their clinical value with that of the semen analysis. The principal objective of a testicular biopsy is to determine whether azoospermia is due to a disorder of the germinal epithelium or to vasoepididymal obstruction.

In many instances such a procedure is not at all necessary, since the finding of small, flabby, atrophic testes in itself indicates that the azoospermia results from an incurable fault in the development of the germinal epithelium. If any spermatozoa happen to be present in the ejaculate, the semen analysis provides a much better index to the quality of the ejaculated spermatozoa than a testicular biopsy, and consequently a far more reliable prognosis. Because the characteristics of the ejaculated spermatozoa mirror the fundamental quality of the germ plasm from which they are derived, and because of the greater clinical applicability of semen analysis in routine clinical



studies, one must depend primarily on a semen analysis for evaluating the fertilizing potential of the male.

There are widely varying seminal characteristics among both the fertile and the infertile which do not necessarily affect their fertility potential to any significant degree. However, a study of many fertile matings indicates clearly that the damage to a sperm population is often more extensive than the observed ratio of abnormal spermatozoa would suggest merely on a percentage basis. Nevertheless, since conceptions occasionally do occur from semen that contains very few normal-appearing spermatozoa, this possibility must always be considered if any normal-appearing cells are present, even though the chances are exceedingly small.

Further, when sperm survival is observed in faulty semen specimens, a small segment of the sperm population will often survive for an exceptional period of time, even as long as eight to ten days. Conceptions will occur from some of these cases in spite of an extremely high ratio of poor quality spermatozoa.

Since, as we have shown, conceptions are occasionally derived from semen specimens containing only a few healthy spermatozoa, all hope should not be abandoned too hastily even though there is a relatively poor seminal picture.

¶ The author has just published a monograph entitled "Sterility" which represents a summation of his work in the field of sterility and fertility. The monograph has been published privately and may be obtained through the author.—A.I.W.

Prepared for Modern Medicine

Diagnostic Value of Testicular Biopsy

FRED A. SIMMONS, M.D.*
Harvard University, Boston

EXAMINATION of biopsy material surgically removed from the human testis establishes at once to the practiced eye the normality or abnormality of spermatogenesis.

When numerous reports agree that 10 to 15% of men complaining of infertility show complete azoospermia on semen analysis, and 33 to 60% show oligospermia, the need for establishing a diagnosis of normal spermatogenesis becomes apparent.

Testicular biopsy, properly secured, fixed, and studied by a trained histologist or pathologist, identifies at once:

1] Men suitable for treatment
2] Those irrevocably sterile
3] The few for whom the very slightest possibility of benefit from treatment exists
4] The efficacy of various therapies, as shown by biopsies made before and after treatment.

Rarely, but statistically, a tumor is found early enough by this means for surgical cure.

Despite the prejudices of certain clinicians, testicular biopsy properly performed is safe, atraumatic, easily done, and extremely diagnostic and, by preventing futile or nonindicated treatment, is also economical.

AZOOSPERMIA

In cases showing complete azoospermia on more than one semen analysis, the diagnosis rests between excretory duct block and failure of the germinal epithelium or, rarely, of the pituitary. Thus, by one simple maneuver, it is possible to determine which patients may respond to treatment and which are hopelessly sterile. This saves the patient considerable mental and emotional strain, time lost from work, and expense.

Infection, congenital anomaly, or trauma, in that order, is the usual cause of blockage of the excretory duct.

Infection is ordinarily gonorrheal, resulting in a bilateral epididymitis. Other causes are rare. The diagnosis is frequently confirmed by the patient's history. What appears clinically to be a unilateral disease may actually be a bilateral block.

In all of 35 consecutive cases of clinical gonorrheal epididymitis, testicular biopsy showed essentially normal spermatogenesis. Today a biopsy before epididymovasostomy is not necessary in cases of clinical gonorrheal epididymitis. As an aid to prognosis, however, a biopsy should be done at operation to confirm normal spermatogenesis.

*Assistant Surgeon, Massachusetts General Hospital; Instructor in Gynecology, Harvard University, Boston.

If anastomosis can be done successfully, the salvage, as represented by normal babies, approaches 30 to 40%. In the current literature, 10 to 60% success has been reported. The fertility of the wife is, of course, assayed first.

Certainly the medical profession owes the infertile couple even a 10% chance by a properly executed surgical attack on an inflammatory obstruction. The husband and wife should at least be allowed to make the decision, instead of being summarily told, "Your case is hopeless!" Cannot a steering committee guide such patients to qualified optimistic surgeons who will operate to create a life on a 10 to 60% gamble?

TABLE 1. BIOPSIES IN 25 CONSECUTIVE CASES OF AZOOSPERMIA*

Diagnosis	*Cases*	*Size of testis*	*Live babies*
Congenital block	6	Normal	0
Bilateral epididymitis	3	Normal	6
Surgical block	1	Normal	0
Sclerosing tubular degeneration	4	Small	0
Complete aspermia	4	Small	0
Severe hypospermatogenesis	5	Small	0
Immature testis	2	Small	2
	25		8

All wives found normal.

As Tables 1 and 2 show, 8 babies were produced in 25 consecutive cases of complete azoospermia, in contrast to only 2 in 25 consecutive cases of oligospermia. We decry the doctor who says azoospermia is a hopeless state!

TABLE 2. BIOPSIES IN 25 CONSECUTIVE CASES OF OLIGOSPERMIA*

Diagnosis	*Cases*	*Live babies*
Normal testis[1]	5	0
Spermatogenic arrest[2]	10	1
Hypospermatogenesis	8	1
Aspermatogenesis	1	0
Miscellaneous[3] (focal atrophy plus normal areas)	1	0
	25	2

All wives studied.
[1]One wife had endometriosis.
[2]Two successful semi-adoption babies; one polycystic ovaries.
[3]Wife has endometriosis.

In 650 testicular biopsies, 14 cases of *congenital absence* of the epididymis, vas deferens, or ejaculatory duct have been discovered. This is only 2%, but 2 of every 100 azoospermic males are immediately released from futile therapy.

We need a surgical attack for these cases by means of artificial spermatocele, which can be aspirated; epididymal fistulas, which can be aspirated; or, possibly, venous or arterial transplants to provide a patent duct. Unfortunately, none of these procedures has as yet been successful in man. It is not beyond the range of possibility to consider a vas deferens bank similar to a bone bank. The solution of this problem presents a challenge.

An increasing number of cases of surgical *trauma* to the vas are

*Simmons, Fred A. "Correlation of Testicular Biopsy Material with Semen Analysis in Male Infertility," *Ann. New York Acad. Sc.* 55:643-656, 1952.

being reported. Trauma may occur in herniorrhaphy and also in surgery for undescended testes, which, in bilateral cases, is now done in the earlier years of life. It is suggested, as a means of prophylaxis, that only one testis be attacked surgically in the infant, since a gonad will often descend spontaneously at puberty if left alone. It is a pity to jeopardize the circulation of the prepubertal vas and testes by overzealous surgery.

More rarely, urethral manipulation by sounds, irrigations, chemicals, catheters, or foreign bodies may damage the delicate pathways of the male reproductive tract. The incidence of trauma to the scrotum and its contents by high-powered missiles, mechanized vehicles, and commando tactics is increasing as modern warfare and transportation accelerate.

One cannot overlook the trauma of the Nazi regime, which deliberately vasectomized hundreds of men. The salvage in reparative surgery among this group reaches 57%.

Testicular biopsy has taught us that a man may have an obstruction of the ductal system for ten to seventeen years and still show active spermatogenesis and fertility when the obstruction is eradicated, usually by surgery. We must, therefore, abandon the defeatist attitude when patients with normal testes exhibit complete azoospermia from obstruction.

ARREST OF SPERMATOGENESIS

Patients with arrested spermatogenesis whose biopsy studies show activity up to or just before spermatid formation may have azoospermia or oligospermia. Until 1950 we classified these patients as irrevocably sterile and advised artificial insemination with donor semen or adoption of a child.

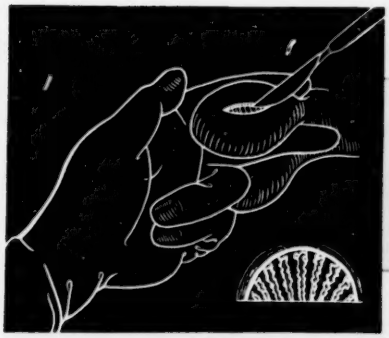
In 1950 Heller and Nelson showed that large doses of testosterone propionate would destroy spermatogenesis in the normal testis, but that six to seventeen months later a rebound phenomenon took place with more sperm than ever being formed. Heckel (1951) has applied this principle clinically and reports 12 babies in 23 cases of spermatogenic arrest.

Here is a fertile field for the application of testicular biopsy. It is too early to state that such heroic therapy is a specific cure, but in these carefully studied and selected cases it indicates promise.* We disparage members of the medical profession who say that there has been no advance in male sterility treatment in the last five years!

The "prepubertal testis" found in males of 19 to 29 years of age with eunuchoid habitus and lack of follicle-stimulating hormones as revealed by urinary assay will respond to treatment. In our clinic 2 babies in 2 consecutive cases have been the salvage thus far, and in 2 other cases, unmarried males, normal spermatogenesis has been re-

*No further reports confirming the value of this method have appeared in the literature. Until they do, it would seem wise to withhold testosterone propionate therapy. Some patients treated with large doses have not as yet shown evidence of the "rebound" but remain in a state of depressed spermatogenesis.—A.I.W.

Technic of Testicular Biopsy



STEP 1

The testis, grasped between the fingers to tighten the skin, is incised 2 cm. to the tunica interna (see cross section). Under novocain or general anesthesia, biopsy is essentially painless.

STEP 2

A 1-cm. incision is made in the tunica interna and is gaped by digital pressure to expose the yellow substance of the tubular mass. Bleeding is rare unless a definite vessel is encountered.

STEP 3

A bead of tubular mass, matchhead size, is expressed and cut off. Tubule mass and testis retract into the scrotal sac when fingers relax. Skin is closed with 1 or 2 black silk sutures.

Adapted from Fred A. Simmons, "Diagnosis and Treatment of the Infertile Male," in *Monographs on Surgery*, Thomas Nelson & Sons, New York City, 1951.

stored, as proved by biopsy and semen analysis. These cases are rare, but require careful evaluation with all our diagnostic armamentaria.

Disorders that do not respond to therapy include:

1] Complete aspermatogenesis—How can a tubule with no germ cells be treated?

2] Hypospermatogenesis—badly damaged tubules with few or no functioning germinal cells, probably congenital or of toxic origin. These cells are already making all the sperms they can.

3] Progressive tubular sclerosis—the well-known Klinefelter syndrome with degrees of gynecomastia, small testes, and a very high urinary content of follicle-stimulating hormone. The tubules reveal few or no germ cells and marked thickening of the basement membrane, frequently obliterating the tubule entirely. These cases usually develop at or after puberty.

4] Complete atrophy, as seen with bilateral mumps orchitis and cases of radiation or excessive heat exposure. No treatment is available for this group.

TECHNIC OF BIOPSY

Like most surgical procedures, the technic of testicular biopsy should be studied in a teaching clinic. The procedure is, however, very simple in most cases.

The patient goes to the operating room without preparation. Pentothal or local anesthesia is administered. The scrotum is then washed, dried, and painted with Scott's solution, which does not burn the delicate scrotal skin. The testis is then fixed between the first and second fingers of the left hand and squeezed until the scrotal skin is taut at the proposed site of incision.

Next, an incision of ½ to ¾ in. is made down to the tunica externa. The escape of a small amount of fluid identifies this advance toward the testis, which may now be seen glistening white in the depths of the wound.

The tunica interna is then incised with a sharp-pointed scalpel for ⅛ to ¼ in. With firmer pressure from the left hand, a bead about the size of the head of a kitchen match containing 6 to 10 tubules extrudes through this tiny incision and is trimmed off with curved iris scissors.

The tissue is immediately placed on filter paper and dropped into fixative, preferably Bouin's solution. Formalin should *not* be used.

The pressure exerted by the left hand is then relaxed and a search made for bleeding. If avoidable, no painful ties or sutures are placed in the testis or its coat. Occasionally a spurter must be ligated with a tiny bite of fine silk.

The skin is closed loosely with silk, a suspensory applied, and the patient goes home. He may miss one day of work. Stitches are removed on the fifth day.

Usually, if the testes are grossly similar, a biopsy of one will give a good picture of the bilateral histology. In infertile males this will probably suffice for prognosis.

Prepared for Modern Medicine

Evaluation of Therapy of the Male

CHARLES W. CHARNY, M.D.*
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SEMEN examination alone or a comparison of the patient's semen with a standard normal is not sufficient for evaluating his fertility status. A man with substandard semen must be classified as fertile if he has fathered a family. On the other hand, a patient with relatively better but still subnormal semen must be classified as infertile if his marriage, to a fertile mate, has remained involuntarily childless.

Fertility in the male implies that a man is capable of depositing into the female genital tract an ejaculate with sufficient fertilizing capacity to result in conception followed by a normal pregnancy and the birth of a normal offspring, provided the female partner is without defect. Inability to do so places upon the man the sole responsibility for a barren marriage. If, however, some abnormality, even though minor, is discovered in the female, it is incumbent upon the gynecologist and the urologist to evaluate the results of their studies and to decide on the relative responsibility of each partner.

ETIOLOGY OF MALE INFERTILITY

Faulty spermatogenesis—Endocrine imbalance is not the only cause of disturbed function of the seminiferous tubules. Congenital disease of the germ plasm accounts for many cases of infertility. Hypernutrition as well as malnutrition may be responsible.

Metabolic diseases, such as diabetes, are frequent causes. Febrile diseases, including the exanthemata, especially when occurring between the age of 10 and puberty, the critical period of tubular development, often permanently damage the seminiferous tubules, resulting in adult infertility. Among the endocrines, the hypophysis, testis, and thyroid are the glands most frequently indicted in infertility. A detailed history, including particularly the age of onset of the endocrinopathy, whether before or after puberty, is very helpful.

The course of treatment and the prognosis depend on the type and extent of tubular damage and the degree of superimposed degeneration. Histologic study of the seminiferous tubules by testicular biopsy is therefore an important part of the diagnostic work-up and a great aid in determining prognosis, and will, of course, differentiate obstructive from nonobstructive lesions. Bio-assay of the urine for quantitative determination of gonadotropin and ketosteroid excretion, as well as basal metabolism and cholesterol studies, may serve as guides to therapy.

Faulty sperm transmission—Ob-

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struction is the cause of faulty transmission of sperm. Azoospermia results if the obstruction is complete and bilateral. Such lesions are generally located in the epididymis and may be congenital or acquired.

If the obstruction is partial, oligospermia occurs. Partial obstruction may appear anywhere in the excretory tract but is most common at the ejaculatory ducts. In such instances the semen volume as well as the sperm count is reduced.

Abnormal biochemical composition of accessory sex gland secretions—Increased viscosity of the semen causes reduced motility, clumping, and early death of the spermatozoa, but the etiology of the condition is obscure. Just what interferes with normal liquefaction of the semen is not known, nor can premature spermatozoan death be blamed on a lack of the nutritive agent fructose, which is abundant in the semen.

Factors leading to improper deposition of semen—Only when the semen is otherwise normal are factors interfering with deposition of the semen significant. A carefully taken, detailed history will often elicit information on sex habits and difficulties which the patient will not voluntarily offer.

Partial impotence and premature ejaculation, both of which are primarily psychogenic, play important roles in limiting the frequency of coitus, often to such a degree that pregnancy is not likely even if other adverse factors are absent. Stricture of the urethra and hypospadias are clinically significant only if the lesions are so advanced that proper deposition of semen in the cervical region is impossible or unlikely.

TREATMENT

Obstructive azoospermia—When obstruction is due to a lesion of the lower pole of the epididymis, successful shunting of the sperm transmission from the upper pole of the epididymis directly to the vas deferens—epididymovasostomy—will restore continuity of the excretory tract. Because the structures are so small, the technic is difficult but, in the hands of an experienced surgeon, the percentage of good results is appreciable.

If the vas deferens also is obstructed or if a lesion exists which precludes an epididymovasal shunt, operative intervention will be of no avail. Similarly, if spermatogenesis also is defective in cases of obstruction, surgery is not indicated.

Obstructive oligospermia—If the lesion lies in the ejaculatory ducts, secondary to a seminal vesiculitis, prostatic massage with vesicular stripping may produce dramatic improvement. In other instances, endoscopic dilatation of the ejaculatory ducts may be beneficial. In some cases the obstruction is caused by inspissated amorphous material in the vas deferens so that lavage by means of a scrotal vasopuncture may improve the semen.

Faulty spermatogenesis—In the category of faulty spermatogenesis are included oligospermia and azoospermia, both of which result from similar lesions, but of different severity.

1] General: Except in those instances in which careful study reveals a definite lesion with a specific remedy, general health measures are useful adjuvants in the management of patients with defective spermatogenesis, as well as of every other infertile patient. Such measures include correction of obvious physical defects, particularly prostatitis and seminal vesiculitis, adjustment of diet with the addition of vitamins when indicated, limitation of alcohol and tobacco, and regulation of sex habits.

2] Hormone administration: Two types of *gonadotropins* are available commercially. These are chorionic gonadotropins, such as Antuitrin "S," Follutein, and APL, and equine gonadotropins, such as Gonadogen. Their use should be limited to patients whose testicular biopsies and excretion studies of urinary gonadotropins reveal a need for them—cases of hypophyseal hypofunction with secondary hypogonadism.

Both gonadotropins should be given in large dosage—the chorionic 1,000 I.U. daily and the equine 80 units daily for a period of six to eight weeks. If improvement does not occur within this period further treatment is not indicated.

Testosterone may be employed as a nonspecific hypophyseal stimulant for patients with reparable lesions of the seminiferous tubules which have not responded to gonadotropin. It is given in large dosage, 50 mg. three times weekly, for an average total of 2,500 mg. or until the spermatozoa have disappeared from the semen. It may also be given in daily doses of 50 mg. for six weeks or in the form of testosterone cyclopentyl propionate, 200 mg. once weekly, for ten to twelve weeks.

The testosterone induces hypophyseal depression and secondary inhibition of spermatogenesis resulting in azoospermia. Its withdrawal then causes hypophyseal stimulation with a "rebound" in spermatogenesis.* In favorable cases, the end result is a sperm count considerably higher than that observed before treatment. Observation should be continued for six months or more after withdrawal of testosterone.

In some instances, the administration of testosterone appears to have a direct stimulating effect on spermatogenesis. The number of cases in which this occurs is relatively small and the indications for its use as a direct stimulant are not clear-cut. When employed in this manner the average dose is 10 to 15 mg. twice weekly.

Desiccated thyroid is a specific therapeutic agent in the hypothyroid case and should be administered in accordance with the patient's needs and tolerance. In such cases, the resulting improvement is quite dramatic. Thyroid is also often employed empirically for the obese with normal metabolism; as much as 3 gr. daily is administered for an indefinite period.

*Not all cases end favorably. Some preliminary reports, not yet published, indicate that failures are common and that some conditions have been worsened by prolonged testosterone therapy. Caution should be used in administering this hormone until further clinical reports appear in the literature.—A.I.W.

Dosage is of course terminated if any intolerance is noted.

Proper management of the hyperthyroid patient will result in rapid improvement of his fertility status. The administration of Lugol's solution, even if only as a preliminary measure, will be followed by a rapid increase in the sperm count.

Insulin and *dietetic regulation* of the diabetic patient need no elaborate discussion here. Rapid improvement of the semen follows the institution of a proper regimen in the previously unregulated diabetic patient.

3] Surgery: Correction of local defects such as varicocele, hydrocele, and spermatocele should be done whenever there is suspicion that spermatogenesis or sperm transmission is adversely affected by them.

Large varicoceles undoubtedly impair the blood supply to the testis, and increased spermatogenesis often follows their removal. Hydroceles generally reflect a disease of the testes or their appendages. Removal of the hydrocele sac alone does not benefit spermatogenesis. Similarly, removal of spermatoceles is not followed by improvement in sperm transmission.

Orchidopexy does not benefit the adult testis which has undergone irreparable degenerative change by the time the infertility becomes a problem. In unilateral cryptorchids, the failure of one testis to descend may cast suspicion on the opposite testis, which may not have developed completely even though normally descended. The management of cryptorchidism in the preadolescent is discussed below.

4] Marital advice: If treatment fails to improve the semen of the infertile male, guidance of the couple, including instruction in proper timing of coitus with respect to ovulation and correct spacing of coitus so as to allow sufficient time for recovery of the semen to an optimum state, may still result in pregnancy. This recovery period is not constant for all men and should be determined specifically in each case by examining the patient's semen specimens collected after varying periods of rest from coitus.

Finally, artificial homologous insemination, employing either the unmodified semen, when the volume is low or the sperm viability reduced, or semen previously concentrated by centrifuging, when the sperm count is low, may yield successful results in the childless couple.

PROPHYLAXIS

There is increasing recognition of the fact that many instances of male infertility are the result of faulty testicular development originating before puberty. The immature testis undergoes three phases before reaching its normal adult status:

Static phase—from birth to age 4
Growth phase—from age 4 to age 10
Development phase—from age 10 to puberty and through adolescence

The development phase—maturation stimulated by gonadotropin secretion—continues through pu-

berty and adolescence. If the gonadotropin stimulation is deficient, the sensitive seminiferous epithelium fails to develop properly. When this condition is encountered in the adult, secondary degenerative changes have already set in, so that the primary lesion is no longer recognizable. Moreover, even if the gonadotropin deficiency is now adjusted, regeneration does not occur because the lesion is fixed and irreversible.

Proper management consists of *early* recognition of the abnormality *in the preadolescent boy* and application of remedial measures at a time when the abnormal state can be more easily modified. Even the available gonadotropins are more effective in the preadolescent. This need for prepubertal treatment has been universally accepted in the management of cryptorchidism. Studies now being made indicate that treatment for many types of adult infertility should also be started in the preadolescent boy. Postponement until adulthood may result in irreparable damage to the seminiferous tubules just as it does in cryptorchidism.

Infertility in the Male

ETIOLOGY

1] Faulty spermatogenesis

2] Faulty transmission of sperm

3] Abnormal biochemical composition of accessory sex gland secretions

4] Factors leading to improper deposition, such as impotence, premature ejaculation, marked hypospadias, stricture of urethra, and the like

TREATMENT

The cause or causes of the infertility having been established, proper treatment consists of applying general and specific measures known to be remedial.

PROPHYLAXIS

Early recognition of abnormal testicular development and prepubertal treatment will often modify the abnormality.

Prepared for Modern Medicine

Vasoepididymal Ductal Obstruction

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THE incidence of obstruction of the vasoepididymal ductal system as a cause of impaired fertility is relatively high. In a series of over 2,100 of my patients with subnormal semen, diagnosis of obstruction of the duct was made in 5%. Undoubtedly the percentage was substantially higher, as a great many others, in whom I believed a similar condition existed, refused the testicular biopsy or exploratory investigation necessary to confirm the diagnosis.

The present series consists of 102 cases of obstruction of the vasoepididymal duct. The diagnosis is based principally on the presence of oligospermia or azoospermia and normal testicular biopsies, 71 cases, and azoospermia and physical findings, 31 cases, including:

a] Unilateral maldevelopment of the vasoepididymal duct, 3 cases

b] Bilateral maldevelopment of the vasoepididymal duct, 17 cases

c] Bilateral vasectomy, 11 cases

There were 73 cases of azoospermia and 29 of oligospermia—4 cases with 20,000,000 to 26,000,000 spermatozoa per cubic centimeter, the remainder with less than 20,000,000 per cubic centimeter.

PATHOLOGY

Obstruction may be single or multiple and may occur in any or all segments of the vasoepididymal ductal system—which, as defined in this paper, includes the ductuli efferentes, duct of the epididymis, and the vas deferens and its terminal portion, the ejaculatory duct. The obstruction may completely or partially block the lumen of the canal. It may involve only a small portion of the duct or extend for many feet.

The lower portion of the corpus and the globus minor are most frequently attacked—about 2.5 times as often as the upper part of the corpus and the globus major. An inflammatory process affecting either the lower portion of the corpus or the globus minor usually involves the other structure as well.

That portion of the vas deferens which adjoins the globus minor is often affected along with these organs, and at operation its fine occluded lumen can usually be seen as a white, hard core less than 1 mm. in diameter. Fibrous obstruction of the more distal portion is much less frequent, occurring in about 25% of the cases that are explored.

The process frequently extends

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outward and includes the sheath and other tissues immediately adjacent to it.

Dilatation of the duct often occurs proximal to the obstruction, but is seldom extreme. The muscular and connective tissues of the wall give it a comparatively unyielding character. These, with the valve-like loops of the duct, which prevent secretions from being forced in the direction of the testis, retard and prevent distention. Stieve gives the diameter of the moderately distended epididymal duct as 2 to 3 mm. I have never seen a diameter of more than 2 mm., even in a case in which obstruction had lasted for over thirty years.

Pathologic alteration in the structure of the testes has never been shown to be caused by obstruction of the vasoepididymal duct. On the contrary, C. R. Moore has found in his experimental work on animals that no change in the testes is demonstrable. Similarly, in 7 of my patients (aged 25 to 31 years) with congenital absence of the vas, the testicular biopsy specimens, as well as the gross appearance of this organ, were normal. It is my opinion that a pathologic process in the testis, noted after ductal obstruction, is the result of some other etiology.

HISTOPATHOLOGY

The architecture of the involved area in general shows varying degrees of fibrosis, vascularity, and round-cell (lymphocytic) infiltration. Usually by the time the area is explored, the process is poorly cellular and may show hyalinization. It may be chiefly submucosal or blend with the stroma so as to involve the entire wall. Either total obliteration or narrowing of the lumen may result. This occurs in varying degrees, with both atrophy and flattening of the lining epithelium.

When dilatation is associated with the obstruction, the wall of the dilated portion of the duct usually shows only a flattening of the lining epithelium microscopically. The muscular and connective tissues present slight demonstrable change except in very extreme cases.

ETIOLOGY

Any inflammatory process affecting the contents of the scrotum may leave a fibrotic area of varying intensity and extent, involving any or all parts of the ductal system.

From the following tabulation it will be noted that the principal causes, gonorrhea, trauma, maldevelopment, and unknown etiology, account for the obstructive lesions in 94% of my cases. The percentages for the different lesions are given.

The relatively high ratio of maldevelopment and vasectomy cases is due to the fact that all such cases were included as cases of obstruction per se, with or without confirmative biopsy or operation. Undoubtedly this proportion would not be so high if the many other patients who refused either biopsy or operation essential to the diagnosis were included.

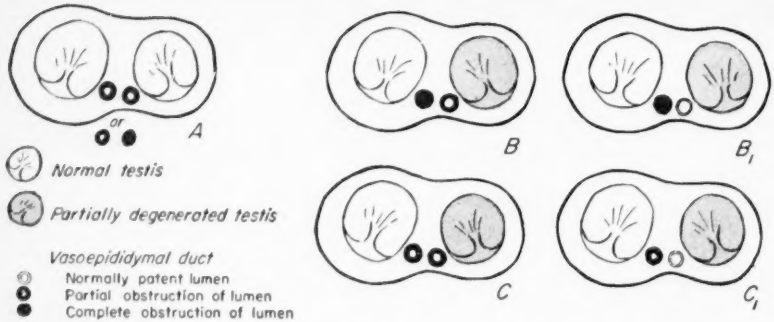


Fig. 1. Types of cases associated with oligospermia that may be amenable to vasoepididymostomy.

Obstruction may cause either oligospermia or azoospermia.* In 28% of this series the blockage produced oligospermia. Normal testicular biopsies confirmed diagnosis in all but 1 case. In 4 instances further verification was obtained at operation. In 1 patient the oligospermia, 400,000 to 2,000,000 per cubic centimeter, was due to partial occlusion of both ducts. After bilateral vasoepididymostomy the count varied from 16,000,000 to 36,000,000 per cubic centimeter and the wife became pregnant.

PATHOGENESIS	CASES	PER CENT
Principal causes		
Bilateral gonorrheal epididymitis	20	19.60
Bilateral trauma (vasectomy, 11 cases; accident, 8 cases)	19	18.63
Bilateral maldevelopment of vas and epididymis	17	16.66
Bilateral, unknown	35	34.31
Combined unilateral lesions	5	4.90
Total	96	94.10
Other lesions		
Unilateral mumps orchitis atrophy and unilateral maldevelopment	1	0.98
Bilateral mumps orchitis and epididymitis	2	1.96
Bilateral nonspecific causes	3	2.96
Total	6	5.90

Obstructive azoospermia is usually due to complete bilateral blockage, but may be caused by unilateral occlusion combined with total degeneration of the seminiferous tubules of the opposite testis.

Oligospermia may be present with bilateral normal testes and bilateral partial ductal obstruction. Various combinations of normal or partially degenerated testes, together with normal or partially obstructed ducts, also may produce oligospermia (Fig. 1).

*The author properly emphasizes a point that has gone unnoticed for many years in the urologic literature—that obstruction may be the underlying cause not only of azoospermia but also of oligospermia. This neglected fact should be borne in mind when evaluating therapy for the infertile male.—A.I.W.

DIAGNOSIS

In patients with azoospermia or oligospermia, the presence of a grossly normal testis and normal testicular biopsy usually is sufficient for diagnosis of obstruction of the vasoepididymal duct. Positive physical findings, such as thickening or nodules on the epididymis or vas deferens, or the absence of portions of these organs helps to localize the site of the lesion. A history of such occurrences as severe local trauma or infection is of course important. A report of gradual decrease in the sperm count over a long period may be obtained.

However, in a large percentage of patients nothing in the history or the preoperative physical findings will point to the diagnosis. In my series this was true for over one-third of the patients.

SURGICAL TREATMENT

Operation to reconstruct the obstructed channels for the transport of spermatozoa is indicated only when it has been determined that a normal testicle is present and that the ductal system has not been sufficiently blocked to preclude restoration of patency.

Preoperatively, in azoospermia and oligospermia, a testicle with normally functioning spermatogenic tissue can be diagnosed only by physical examination and testicular biopsy. The extent of the disease process in the ductal system often can be determined only at operation. Not infrequently, however, fibrosis of the duct sufficient to cause blockage of the lumen may be recognized by preoperative inspection and palpation.

The type of operation to be performed depends upon the location of the lesion. Examples of operations used are:

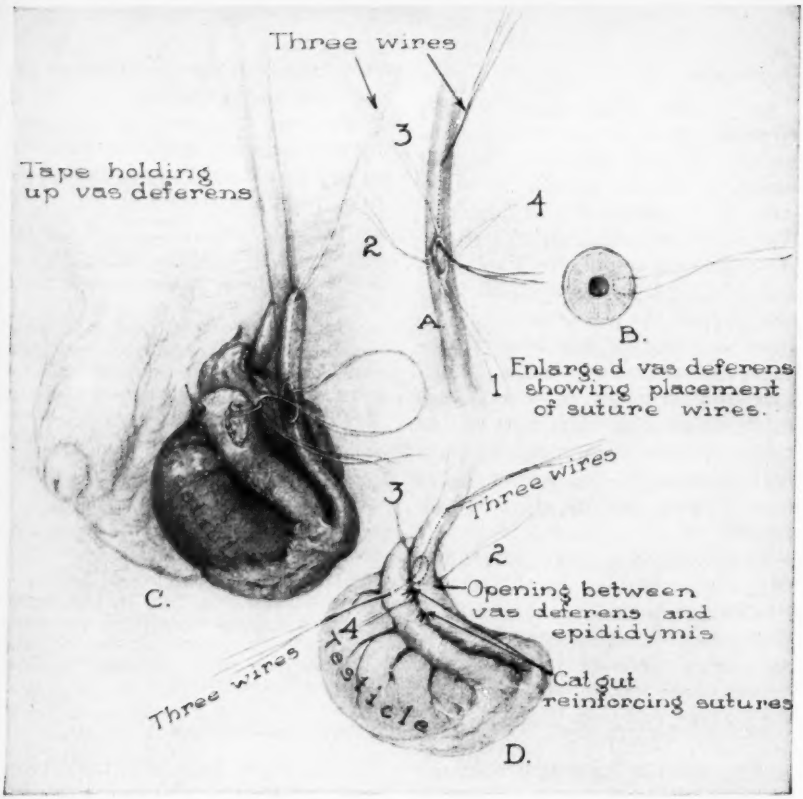
- *Epididymis*—bypassage of the obstruction and anastomosis of the vas deferens and the patent portion of the epididymis
- *Vas deferens, scrotal and inguinal*—resection of the fibrosed area and anastomosis of the cut ends of the vas over a splint of silkworm gut or stainless steel wires. The splint is removed nine or ten days postoperatively.
- *Pelvic vas*—inaccessible
- *Ejaculatory duct, partial obstruction*—dilatation through the endoscope
- *Cross or contralateral lesions*—cross anastomosis, that is, anastomosis of a normal vas of an atrophied testis to the patent portion of the blocked duct of the opposite normal testis.

EPIDIDYMOVASOSTOMY

The basic principle underlying reestablishment of patency of the ductal passageways is the production of a permanent ostium between the patent portions of the ductal system. This procedure bypasses the obstructed area.

The first successful anastomosis was reported by Martin in 1902. The splint modification was devised by me in 1945, and is, in my experience, a considerably more successful procedure than the Hagner-Martin. It differs from the latter only in the use of the splint and of stainless steel instead of silver wire sutures.

The testis and adjoining structures are delivered through a rou-



Courtesy of Surgery, Gynecology and Obstetrics

Fig. 2. (A) The group of three wires has been passed through the oval incision in the vas, up the lumen of the vas, and out through its wall. The four wire sutures *(1, 2, 3, 4)* to make the anastomosis are shown. (B) Diagrammatic cross section through the vas showing depth of anastomotic suture wires in its wall. (C) The oval fenestra has been cut in the globus major. The needle carrying the fistula wires from the vas has partly been passed through the globus major. (D) The anastomosis between the vas deferens and epididymis has been completed. The three wires which temporarily maintain the fistula are shown. Their course is indicated by the dotted line. The four anastomotic suture wires have been passed and tied. Three of them have not been cut and are shown.

tine anterior scrotal incision (Fig. 2). An area on the vas distal to the obstruction is selected for the site of the anastomosis. The area is incised and tested for patency toward the urethra by injection of 4 cc. of methylene blue. An oval foramen 3 by 4 mm. is cut into the posterior lateral surface of the epididymis.

The incision used must include some of the loops or tubules of the duct.

The exudate from the cut tubules is immediately examined microscopically and, if spermatozoa are present, a splint of 3 stainless steel wires is passed through the lumen of the distal segment for about 2 cm. and then through the wall and out the scrotal skin. The lower ends of the wires are passed through the incised foramen of the epididymis and out the other side through the serous coat and scrotal skin.

The cut edge of the distal segment of the vas is sutured to corresponding points on the foramen in the epididymis by 4 stainless steel wires. The ends of the splint wires are shotted. The wires are removed after twelve to fourteen days.

The results cannot be satisfactorily evaluated until one year after the operation, as spermatozoa may not appear in the ejaculate or fibrous tissue may block the duct within this time.

The technic for repair of previous vasectomies is simpler (Fig. 3). The scar tissue is dissected from the cut ends of both segments of the vas. After the lumen of the distal segment has been found to be patent through the ejaculatory duct and the presence of spermatozoa from the lumen of the proximal segment has also been demonstrated, splint wires are inserted through the lumen of both segments. Suture wires fasten both segments together over the splint. The splint wires are passed through the skin and shotted. These are removed after nine days.

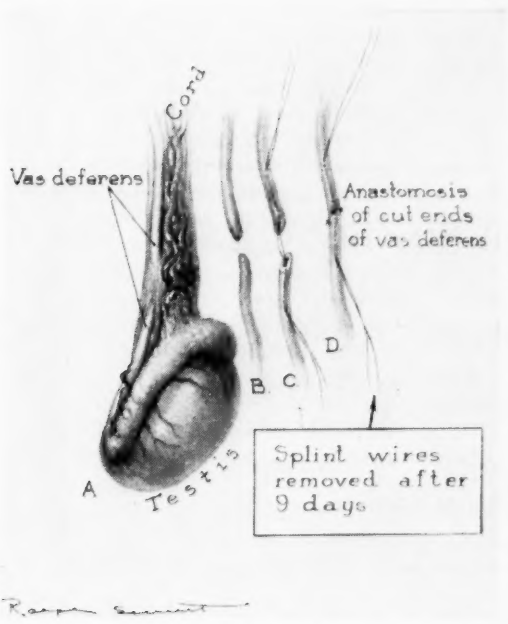


Fig. 3. Anastomosis of vas deferens following vasectomy. (A) Severed segments of vas with bridge of scar tissue. (B) Segments freed of scar tissue. (C) Splint wires in place. (D) Segments approximated by 3 wire sutures. Dotted line, course of splint wires.

According to reports by different observers, the percentage of successful epididymovasostomies, as evidenced by active spermatozoa in the semen, varies from 20 to 65%. The percentage of pregnancies ob-

tained varies from 10 to 42%. My results show approximately 30% successful operations, judging by presence of spermatozoa in the semen, and 16%, by the incidence of pregnant wives.

The percentage of successful operations upon previous vasectomies is much higher. Of 11 that I have done, using a splint of steel wires, spermatozoa were present postoperatively in all cases. Of the 11 wives, 2 had previously unrecognized pelvic lesions which precluded pregnancy. In the 9 others, 2 pregnancies occurred. This represents success in 22% of cases when the wife was capable of conception.

Although the percentage of successful results from any of these types of anastomosis is not high, the minor nature of the operation, the absence of serious after effects, and the short period of incapacitation warrant the attempt to remedy an otherwise barren marriage by this means.

Prepared for Modern Medicine

Cervical Factor in Infertility

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THE cervix is important in the problem of infertility. Its influence is manifested by anatomic and functional characteristics.

Such conditions as position in the vaginal canal, hypoplasia, stenosis, tumors, angulation, and stricture have received considerable attention in the past fifty years and will not be discussed here. Our present concern is with the functional characteristics, as represented by the cervical mucus, especially in relation to the seminal fluid. The ultimate problems are migration of sperm through the mucus and the chemical action of the mucus on the sperm and of the spermatozoa on the mucus.

Mucus is secreted by the glands lining the cervical canal and probably presents an admixture of cervical and uterine secretions. Both its physical and chemical constituents are under hormonal control. When midcycle approaches, viscosity decreases, diminishing to a minimum at the time of ovulation. As the cycle progresses into the lutein phase, the viscosity increases, to reach a maximum during pregnancy.

In general, the lesser the viscosity, the greater the ease of penetration by sperm. Seminal fluid contains an enzyme system capable of hydrolyzing cervical mucus, thus further promoting the progress of spermatozoa. Hence, failure to decrease the viscosity of the mucus, or a deficiency of the enzyme system, may prevent or delay the passage of sperm into the uterine cavity.

The *p*H of cervical mucus is alkaline, about 7.4. Any increase in acidity, as in the presence of endocervicitis, may prevent the progress of sperm through the cervix.

The ability of spermatozoa to penetrate this mucus can be chemically demonstrated in vivo by the Huhner test and in vitro by means of the Miller-Kurzrok test. Demonstration of such penetration is important in the diagnosis and treatment of sterility.

Aside from penetration, one also occasionally observes that the sperm cells have lost their motility. This may denote an inherently low survival level in the spermatozoa or a "toxic" action by the cervical mucus. A parallel test with seminal fluid alone would demonstrate the survival capacity of the sperm.

Failure of sperm to penetrate cervical mucus is best treated by modification of the mucus. We know of no method of increasing the penetrating power of spermatozoa.

One of the commonest causes of failure of penetration is endocervi-

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citis. We treat this condition now with antibiotics, using a combination of 400,000 units of penicillin and 1 gm. of dihydrostreptomycin. Daily injections are given on five successive days immediately after the menstrual period. Equally good results may be obtained by daily insertion of a vaginal tablet or suppository containing 100 mg. of terramycin throughout the cycle. Repetition of this treatment may be necessary for two or three successive months. Trichomoniasis and moniliasis should receive specific therapy.

As stated previously, the amount and character of the cervical secretions are controlled by hormones. Small daily doses of estrogens, 0.02 mg. of ethinyl estradiol or 1.25 mg. of estrone sulfate, during the first half of the cycle will increase the flow of a thin mucus.

Occasionally the mucus is so gelatinous as to completely block the progress of sperm. The etiology of this thick mucus, when no evidence of chronic endocervicitis is seen, is still in doubt, though many theories have been advanced. Consequently, the treatment of this condition is not satisfactory. Repeated cervical cauterizations and conizations do not give the desired results despite reports to the contrary. Some small success has been obtained from local application of the enzyme caroid to the cervical os at the time of ovulation.

The "fern phenomenon," popularized by Campos da Paz of Rio de Janeiro, may throw some light on the chemical content of the cervical mucus, but aside from the fact that the mucus will dry in characteristic fern crystallization varieties and that this is related to estrogenic function, little else is known. Apparently, spermatozoa can penetrate mucus that dries in fern formation, but estrogen administration will not always cause such formation.

In my opinion, dilation of the cervix produces an increase in the output of follicle-stimulating hormone in the urine and, if properly timed, may lead to ovulation. This would explain why the mere passage of a uterine sound is occasionally followed shortly afterward by pregnancy.*

The role ascribed to cervical mucus has been passive. Perhaps it is also active. The mucoproteins on hydrolysis yield amino acids and sugars that may contribute to the source of energy for sperm. Furthermore, the column of mucus may serve as a "filter" for spermatozoa, allowing the most active to pass through and retaining the less active and morphologically abnormal.

That the normal cervix has an important part in sperm migration is without doubt. Likewise, the abnormal cervix can be a really hostile force against the entrance of sperm cells. Much remains to be learned regarding the role of cervical mucus in preventing the ingress of actively motile spermatozoa.

*Such a procedure has long been known to evoke ovulation in the rabbit. The occurrence in human beings is not generally established.—A.I.W.

Prepared for Modern Medicine

Tests for Tubal Patency

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THE basis for all tests of tubal patency is the anatomic fact that the inner portion of the female genital tract opens below into the vagina and above into the abdominal cavity.

Direct exploration of the cervical canal and uterine cavity by probe and sound was practiced long before this century. But the more inaccessible fallopian tubes could not be similarly investigated except by laparotomy. To circumvent this rather drastic procedure for the sole purpose of determining tubal patency, one had to resort to other methods, two of which were made available between 1910 and 1920.

The oldest nonsurgical method is injection of fluids into the uterine cavity under a pressure adequate to force them through the fallopian tubes into the peritoneal cavity. The other procedure is uterotubal insufflation of gas. For the past thirty years these two methods, with certain improvements, have remained the standard tests for determining tubal patency and nonpatency.

FLUID INJECTION

Fluids used for intrauterine injection either may be radiopaque or may permit roentgen rays to pass through them without casting shadows of the tubal lumen on the film. The latter fluids, first to be employed, were isotonic salt solutions. Lelorier apparently employed such fluids as early as 1912. He used 20 cc. of the solution and claimed that if only a small portion of this amount regurgitated after removing the uterine cannula, the tubes were freely traversed by the fluid. If an appreciable pressure was required and most of the salt solution escaped from the external os, tubal obstruction was indicated. It was soon realized that this method lacked reliability.

A much more dependable method was offered by hysterosalpingography, which has the superior advantage of demonstrating roentgen-ray shadows of the lumen of the tubes when the tubes are freely open. Nonpatency, if encountered, reveals the first proximal point of obstruction. Failure to visualize the tubal lumen, however, is not always conclusive of organic obstruction at the uterotubal junction. In such cases, uterotubal spasm must be ruled out by appropriate measures.

The advantages of roentgen-ray visualization over nonopaque salt solutions led to the universal adoption of the radiopaque substances as a test for tubal patency. The first roentgen-ray opaque medium em-

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ployed was bismuth emulsion. Collargol was used between 1913 and 1915 and was succeeded by the halogen salts, chiefly of iodine and bromine; compounds of thorium were also experimented with until about 1923. Lipiodol and other iodized oils were introduced at this time and are still widely employed. Some fifteen years ago, the crystalloid iodine solutions began to find favor—Skiodan in acacia, Viscorayopake, and modifications of the latter, as well as of the iodized oils.

Except for bismuth and barium, the author at various times has used practically all these radiopaque media.

UTEROTUBAL INSUFFLATION

In 1919 oxygen was employed for uterotubal insufflation, the first gas to be so used. Gas was a sharp departure from radiopaque substances, its *raison d'être* being to avoid tubal inspissation, which had been observed in the fallopian tubes after injection of chemical substances into the uterine cavity.

Oxygen cast no shadows of definite diagnostic significance within the uterine cavity and practically none at all within the tubal lumen, but could be detected radiologically by contrast with the lungs above and the liver below the diaphragm, if large enough amounts passed through the tubes and produced an appreciable subphrenic pneumoperitoneum. Without resorting to the use of x-rays, the physician could, with the employment of oxygen, diagnose the presence of a subphrenic pneumoperitoneum by the patient's complaint of shoulder pains, which are pathognomonic of tubal patency. Failure to produce shoulder pains is proof that the tubes are obstructed.

Because the shoulder pains produced by oxygen tended to last for several days, oxygen was replaced by carbon dioxide. This gas, being rapidly resorbed, minimizes the referred sensations in the shoulders. Carbon dioxide has been used as the gas of choice in the Rubin test since 1921.

The sign and symptom of shoulder pain, however, was not relied upon entirely for the diagnosis of tubal patency by the method of uterotubal insufflation. There were the additional diagnostic factors of manometric pressure and the pattern of the "tubograph" produced on the kymograph, which was added to the insufflation apparatus in 1925.

Contraindications are the same for both methods: [1] signs of active or subacute pelvic infection; and [2] presence of pelvic tenderness elicited by bimanual examination.

Kymographic uterotubal insufflation has been preferred by many gynecologists as the means of testing for tubal patency. Hysterosalpingography has a more useful scope in demonstrating intrauterine lesions and other anomalies.

Insufflation of carbon dioxide has a number of advantages, the chief of which are:

- Safer and more convenient repetition when necessary for diagnostic or therapeutic purposes
- Possibility of determining degrees

of obstruction and estimating them in relation to the size of the ovum*

• Avoidance, in cases of *partial tubal blockage*, of foreign body granuloma formation, which not infrequently follows injection of the iodized oils and may lead to *total occlusion*.

The incidence of infection is much lower after a kymographic uterotubal insufflation with carbon dioxide than after the injection of iodized oils. The former is thus the favored method in the vast majority of sterility cases.

For the specific purpose of clinical determination of tubal patency, uterotubal insufflation should be used first and then repeated if patency is not demonstrated by the first test. Should operative intervention be considered, resort to hysterography is useful [1] to corroborate the point of obstruction arrived at by insufflation, and [2] to establish the presence or absence of an intracavitary uterine lesion which may, if necessary, also be dealt with surgically.

A word of caution in connection with gas insufflation is always necessary. *The use of air* should be avoided, though this agent was previously recommended by others because of ready availability and simplicity. Air embolism was encountered by several operators and resulted in a few fatalities.

I have never used air to test for tubal patency, preferring carbon dioxide, which has not been known to produce fatal embolization. The explanation for this most important discrepancy is found in the physical property of carbon dioxide, which is somewhat more soluble than air and combines with fluid to form carbonic acid. Air, like nitrogen and oxygen, is practically insoluble under the same conditions of pressure and temperature.

During the last thirty years many modifications have been reported in the types of insufflation apparatus, uterine cannula, and various radiopaque agents used.

Of the agents recently introduced for testing tubal patency, phenolsulfonphthalein (PSP) has received some attention. Before this urologic dye was used, methylene blue and indigo carmine were employed for the same purpose during laparotomy and culdoscopy. The urographic dyes are to be differentiated from crystalloid iodine salts such as Uroselectan, Neo-Iopax, Diodrast, Hippuran, and others, as used in excretory urography and whether injected into the veins or through the uterus and into the peritoneal cavity from which they are absorbed and excreted.

Indigo carmine was tried clinically by the author and abandoned as unreliable in the presence of partial or complete tubal obstruction. It was also not without untoward effects, chiefly irritative.

PSP shares the same disadvantages as indigo carmine, requiring thirty minutes for a result which is not altogether reliable. According to E. M. Rossett, only 14 of 25 tests were correctly correlated to the actual condition of the tubes, 2 being negative and 12 positive. It has the disadvantage of requiring retention of the cannula within the uterus for ten minutes, which is an-

noying to the patient. Peritoneal irritation persists much longer than is desirable.

The chief limitations of PSP are that, unlike radiopaque fluids, it fails to visualize the lumen of the tubes, does not indicate the point of obstruction and, therefore, will not show whether one or both tubes are patent or which one, if either, is obstructed. Furthermore, PSP is incapable of demonstrating the presence or absence of tubal peristalsis or the various degrees of tubal stricture.

Too crude and unreliable for clinical application is the introduction of graduated bougies into the uterine cavity, thus allowing air to enter the fallopian tubes, like that which sometimes follows the insertion of a uterine cannula with the patient in knee-chest position for the purpose of producing a subphrenic pneumoperitoneum.

Against these "stunt" technics may be presented the simple method employed long ago which consists of using a Record syringe of 50- to 100-cc. capacity filled with carbon dioxide and attached to a manometer. If auscultation is employed and the manometer is watched during the carbon-dioxide injection, which is made slowly and carefully, some important diagnostic desiderata can be realized.

But this simple method of insufflation only serves to emphasize the superior advantages of kymographic uterotubal insufflation with a uniform and automatically regulated flow of 60 to 30 cc. of carbon dioxide a minute. In contrast to the uncertainty of manual force applied to the syringe during the carbon-dioxide injection, the apparatus designed for kymographic uterotubal insufflation operates with scientific accuracy.

Kymographic uterotubal insufflation and hysterosalpingography, having stood the test of time, will continue to be used until some other as yet unpredictable method can be found to supersede them. At present, carbon dioxide appears to fulfill all the requirements of an ideal gas for uterotubal insufflation. Whether supplied in small tanks of compressed gas or in sparklets, which are always and everywhere available, it satisfies the criteria of a safe, innocuous, rapidly resorbable gas.

There is, however, room for improvement in the development of the ideal radiopaque substance. A combination of crystalloid iodine solution with a thickening agent such as methylcellulose or polyvinyl or some blood substitute appears to be a good approach to the much desired radiopaque medium.

Prepared for Modern Medicine

The Gynographic Survey

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A SIMPLE procedure involving simultaneous use of the Rubin test and instillation of a radiopaque medium eliminates the need for subjecting the patient to two separate and painful experiences in a sterility study. With the use of this method, which I term the gynographic survey, the knowledge derived from tubal insufflation with carbon dioxide, together with additional information obtained by outlining the genital tract with a radiopaque medium, leads to a prompt and accurate diagnosis.

It is not within the province of this short paper to argue whether carbon-dioxide tubal insufflation is as good as, or better than, hysterosalpingography. Both these tests have advantages and disadvantages.

TECHNIC

Employing the author's apparatus the gynograph (Fig. 1), a preliminary gaseous insufflation is performed. Small amounts of an opaque substance are then instilled into the uterus under fluoroscopic visualization. Radiographic exposures are made as the medium fills the uterus and fallopian tubes.

Finally, without moving the patient and by the simple flick of a switch, carbon-dioxide gas is once more instilled. This secondary Rubin test forces the viscous medium through the distal ends of the tubes and causes immediate dispersion of the opaque substance, allowing for the exposure of the final and control film (Fig. 2). All this is automatic, with a self-retaining cannula and a self-controlled pressure device, leaving the examiner's hands free for fluoroscopy and radiography.

Fig. 1 The gynograph in place for testing

With the simultaneous use of the Rubin test and hysterosalpingography, the physician can obtain a definitive picture of the internal genital tract without guesswork or hypotheses. If the gas enters the abdomen, one need not wonder whether one or both tubes are patent; the roentgen pictures will furnish definite proof of the tubal status. If no gas enters the peritoneal cavity and bilateral tubal occlusion is evident, the plates will

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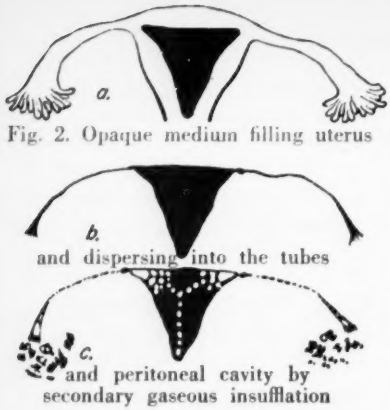

Fig. 2. Opaque medium filling uterus

immediately reveal the site of the blockage. If uterotubal spasm occurs, the combined use of gas and opaque viscous medium affords a much better chance of overcoming the spasticity than would either method used singly.

Moreover, with the combined technic, pathologic conditions such as double uterus, polyps, intracavitary fibroids, and so on are never overlooked, and the etiology of the infertility is more swiftly discovered.

THERAPEUTIC VALUE

In the past, various claims have been made for the therapeutic value of the Rubin test and hysterosalpingography in cases in which sterility is due to tubal closure. I can unhesitatingly state that no method, whether the Rubin test, hysterosalpingography, or a combined gynographic survey, can secure patency of a solidly closed, clubbed tube or a tube deeply enmeshed in dense and thickened peritoneal adhesions. The vast majority of investigators will agree.

On the other hand, if the pathologic state consists of thin velamentous peritubal adhesions or if it is intratubal with thin-walled obstruction, both gaseous insufflation and hysterosalpingography are of inestimable value therapeutically. It would naturally be expected that a technic which employs both gas and a viscous fluid medium would have even a better chance of releasing some of the fine tubal adhesions and obstructions.

I have collected quite a sizable series of cases in which comparisons can be made of the results of the Rubin test alone, hysterosalpingography alone, and the combined method. The data thus obtained reveal that pregnancy occurs much more frequently following the combined technic than after either the Rubin test or hysterosalpingography used alone.

The Rubin test and hysterosalpingography, performed simultaneously, yield the most satisfactory information regarding the female uterotubal tract. Not only is the combined method a superior diagnostic means of studying the female genital tract, but the therapeutic results show a higher percentage of pregnancies than when carbon-dioxide gas or opaque medium is employed alone.

¶ A detailed account of the gynograph may be found in *Radiology* 56:104, 1951 and in *Fertility and Sterility* 1:321, 1950. Stein has devised a technic known as gynecography. In this procedure the patient is subjected to continued carbon-dioxide insufflation causing a pneumoperitoneum. Then an opaque medium is instilled into the uterotubal tract and roentgenograms are made. In this fashion, shadows of gas about the ovaries often disclose ovarian disease in addition to uterotubal abnormalities. This is not an office procedure.

Prepared for Modern Medicine

Interpretation of Basal Temperatures

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THE clinical application of basal temperature changes in the study of ovarian function has met with wide acceptance. This simple physiologic phenomenon provides a useful tool for the interpretation of normal and abnormal ovarian activity. The purpose of this discussion is to familiarize the readers with the method and to point out where it can be applied.

Normal body temperature fluctuations occur in healthy men and women. The temperature is at the lowest level during sleep and immediately on waking in the morning. The temperature recorded at this time is known as the basal temperature. The level increases on arising and resuming the day's activities and remains elevated throughout the waking hours. Physical and mental exertion, eating, exercise, and unusual stimuli of any kind will cause a rise of temperature.

If a healthy man records his waking temperature on a suitable graph each morning for a month, the daily fluctuations will be very small. The basal temperature graph of a healthy woman during a typical ovarian cycle shows a characteristic pattern. It is at a low level during the menstrual days, reaching the lowest point at the end of the bleeding period. The temperature remains depressed during the preovulatory phase, when follicle activity produces estrogens only, but rises during the ovulatory phase of the cycle and maintains an elevated level during the thirteen or fourteen days that the corpus luteum is functioning. Twenty-four or thirty-six hours before the onset of menstruation, the basal temperature begins to decline, and this drop continues during the menstrual phase (Fig. 1).

Thus, the basal temperature graph in the mature woman has been labeled as biphasic in character: a low preovulatory phase and an elevated postovulatory phase. It has been demonstrated by the author and his associates and by others that the temperature rise and its maintenance during the postovulatory phase are induced by the production of progesterone by the corpus luteum. The typical temperature elevation is reproduced by the administration of progesterone to young castrate women as well as to individuals with primary ovarian failure (Fig. 2).

If pregnancy occurs, the premenstrual drop does not take place and the temperature level remains elevated for more than half of the pregnancy. Thus, the failure of

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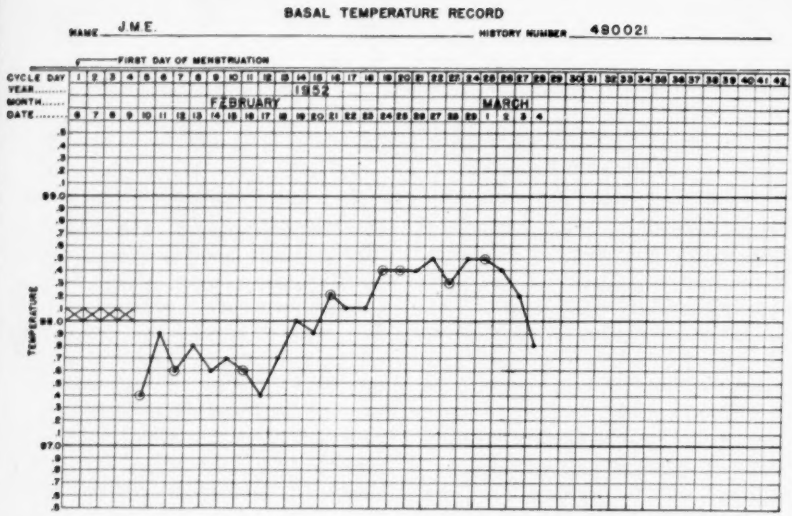

Fig. 1. Basal temperature record of a young woman who has regular menstrual cycles of twenty-seven to thirty-one days. Note the low level of temperature in the preovulatory phase prior to cycle-day 12 when it reaches its lowest point. The progressive rise in temperature during cycle-days 13, 14, and 15 is the transitory phase during which ovulation occurs. The elevated temperature is maintained in the postovulatory phase for thirteen or fourteen days, the life span of the corpus luteum. The drop in temperature before the onset of menstruation denotes the regression of the corpus luteum.

the basal temperature to drop at the end of the cycle coincidentally with the failure of menstruation to begin is an early sign of pregnancy. In the care of women for infertility this early sign of a possible pregnancy is important (Fig. 3).

OVULATION

The transitory phase of the basal temperature from its low preovulatory to its high postovulatory level is associated with ovulation. The pattern of this transition varies considerably in different women and, to some extent, in the same individual.

The temperature may rise precipitously over a twenty-four to thirty-six-hour period, thus providing a sharp end point denoting the ovulatory period, or it may mount slowly, sometimes in stepladder fashion, the rise spread over seventy-two hours or even longer. The varying character of the transitory phase may be due to the pattern of corpus luteum function.

It would be extremely interesting if it were possible to pinpoint the time of ovulation on the basal temperature graph as it is being prepared from day to day. Ovulation has usually been considered to

occur at the lowest point in the transitory phase on the basal temperature graph. Thus, the lowest level of temperature preceding the ovulatory phase has been regarded as the period of ovulation. This end point, although extremely important in the study and treatment of ovarian function, is not definite. Conceptions have occurred twenty-four and forty-eight hours after the onset of the rise (Fig. 4). It is thus likely that ovulation may occur at a somewhat later interval.

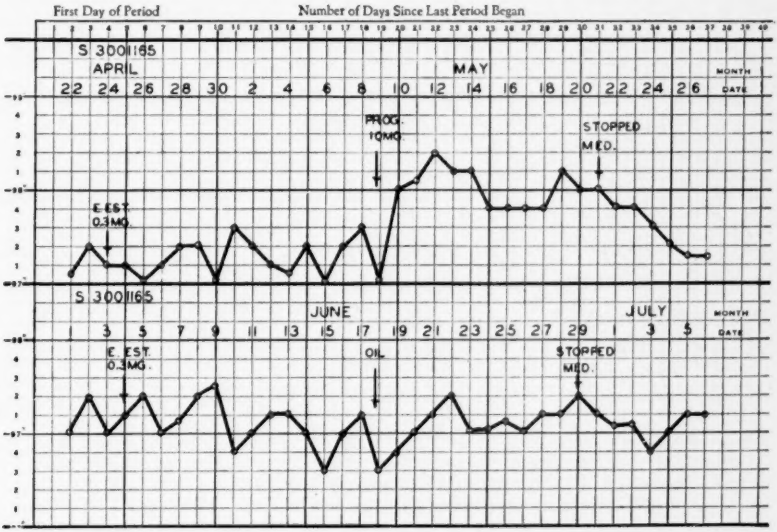

Fig. 2. Rise of the basal temperature and its maintenance during the period of administration of progesterone to a patient with gonadal failure.

In the clinical application of basal temperature to the study of ovarian function, it suffices to regard the period of transition in body temperature as the fertile period. Thus, for practical purposes, it may be taken to extend over two or even three days. Women who wish to conceive should be instructed to have coitus during this temperature shift, not just once, but on several occasions. When the husband's fertility is low because of sperm deficiencies, it is well to restrict coitus to that period when the temperature shifts from its low preovulatory to its high postovulatory level. This may increase the likelihood of pregnancy.

The study of ovarian function is an important part of every sterility investigation. Women who have normal, regular menstrual patterns usually ovulate regularly. However, those who have irregular menstrual periods or atypical episodes of bleeding may ovulate at irregular intervals. Lastly, women who bleed at long intervals rarely ovulate.

There are several methods of determining ovulation in women. The endometrium mirrors the endocrinal changes in the ovary. An endometrial biopsy taken at the onset of bleeding by a suction curet or biopsy punch and prepared histologically will show progestational changes if the patient has ovulated and has developed a corpus luteum. On the other hand, the absence of a typical secretory endometrium is fairly positive proof that ovulation did not precede menstruation.

The second method of demonstrating ovulation is the quantitative determination of urinary pregnandiol. Only minute amounts of the pregnandiol complex are excreted in the urine before ovulation. The development of the corpus luteum results in the production of progesterone, which is metabolized and excreted in the urine as pregnandiol. From 5 to 10 mg. a day is found in the urine during the thirteen or fourteen days of the ovulatory phase. Thus, the pooling of two days' urine output collected during the week preceding menstruation will yield 10 to 20 mg. of pregnandiol.

The most practical method of studying the ovarian cycle is by the use of basal temperature records. It has the advantage of simplicity

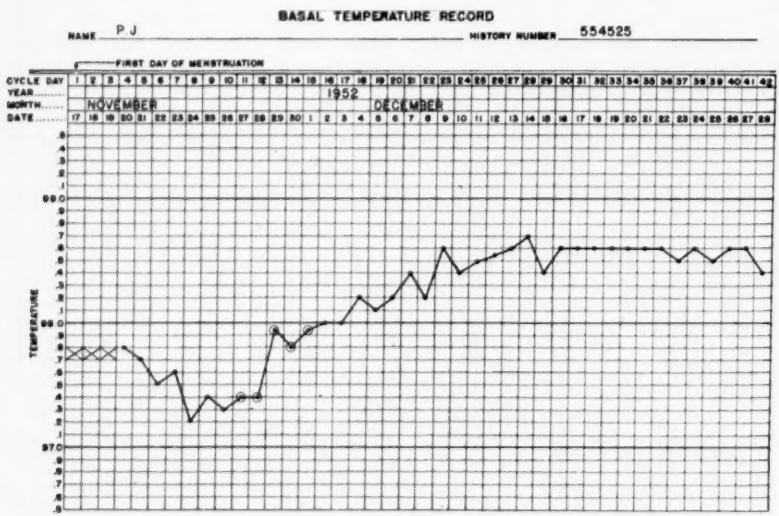

Fig. 3. Basal temperature record of a patient who could not conceive over a five-year period. The husband had a rather severe sperm deficiency. Coitus was restricted to the period of temperature transition from its low to its elevated level. Note the abrupt rise in temperature on cycle-days 12 and 13. Ovulation probably occurred on day 11 or 12. The maintenance of the elevated level of temperature after cycle-day 30 is reliable evidence of pregnancy.

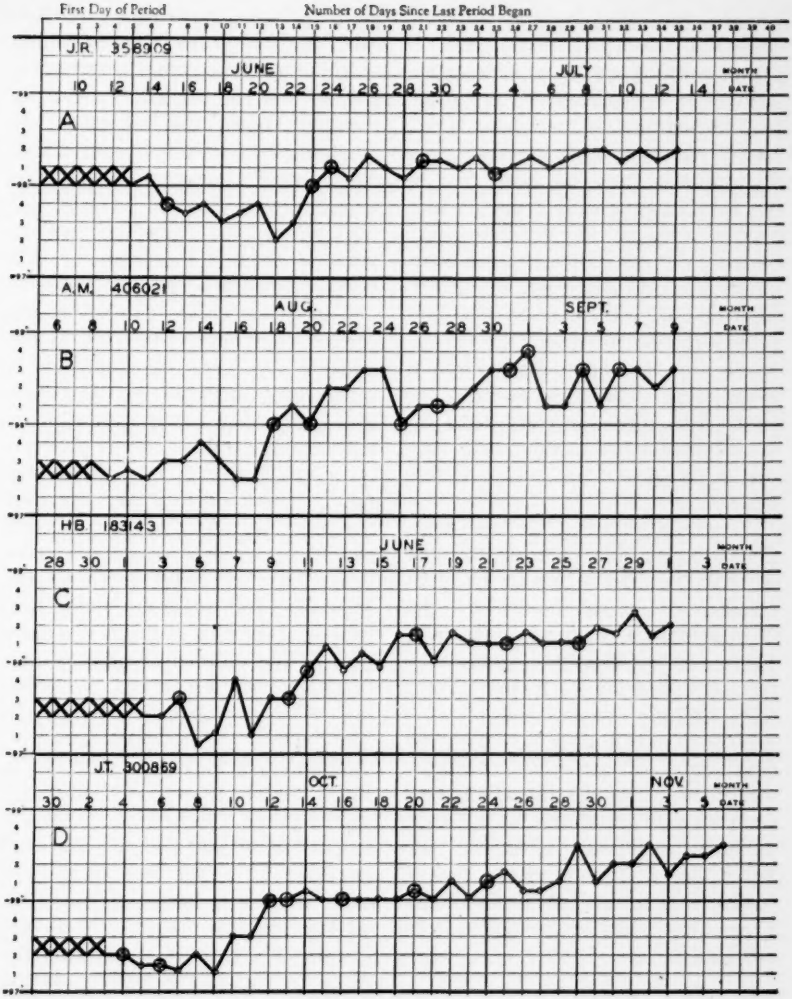

Fig. 4. Basal temperature graphs during the months of conception of each of 4 women studied for infertility. Note that the fruitful coitus in each instance occurred after the temperature had reached its lowest point during the transitory phase of the cycle. In D, fertilization probably occurred near the peak of the rise. Thus it is difficult to pinpoint ovulation on most temperature graphs and the period of transition from the low to the high level should be regarded as the time of ovulation.

whereas the other methods involve laborious laboratory procedures.

An even more important asset is that the occurrence of ovulation and corpus luteum formation is reflected in the daily temperature fluctuations. Thus, the transition of the basal temperature from its low preovulatory to its elevated postovulatory level represents the ovulatory period. Although the exact time of ovulation cannot often be pinpointed on the graph, its occurrence can be confined within a twenty-four to seventy-two-hour period. Thus, the transitory zone on the normal basal temperature record is the period of optimum fertility.

Continuation of an elevated temperature beyond the usual thirteen or fourteen days is due to the elaboration of progesterone by the corpus luteum, whose regression is prevented by chorionic gonadotropin produced by early pregnancy. Very early in the gestation, however, the chorionic cells take over the production of estrogens and progesterone. Although the amount of progesterone continues to increase as the pregnancy advances, the basal temperature tends to seek a lower level in the latter half of the pregnancy. There is no explanation for this.

KEEPING A RECORD

Only a few simple instructions to the patient are necessary for preparing an informative basal temperature record.

An oral thermometer with clear markings should be used so that the scale can be read easily. Any good thermometer will do, but the usual household fever thermometer is difficult to read, since the scale is long and the markings are close together. Basal thermometers are available with a short scale which can be read more easily. The scale extends from only 96 to 100° F., well within the range of healthy persons. Such a thermometer is a good investment for the patient.

The thermometer and a suitable record sheet should be kept at the bedside. As soon as the patient wakes each morning she places the thermometer in her mouth, obtains the reading, and records it promptly on the graph. If intercourse has taken place during the previous evening the dot on the record should be circled. After a woman has taken her basal temperatures regularly for several weeks, the process becomes routine, a simple part of the pattern of getting up.

There is no advantage in recording rectal or vaginal temperatures. The former are no more accurate, although somewhat higher. It is much simpler to take oral readings.

The graph will be more informative if the patient records her temperature at about the same time each morning. Irregular hours as well as physical and emotional disturbances are reflected in the temperature curve. The patient should be asked to record major variations in her normal pattern of living so that the physician can better interpret the graph.

One of the most common errors made by a woman who is keeping a temperature graph is the failure to understand that cycle days and

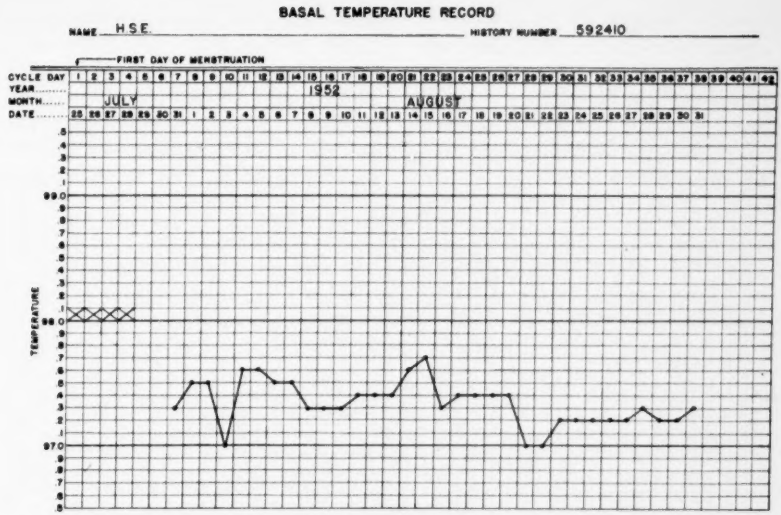

Fig. 5. Basal temperature record of one cycle of a 45-year-old woman with increasingly irregular bleeding periods. This record, typical of an anovulatory cycle in the climacteric, shows minor fluctuations of the basal temperature from day to day but no evidence of ovulation.

the days of the month are not synonymous. She should be instructed to begin her temperature recording on the *first morning of the menstrual period*. This is cycle-day 1. She continues to record basal temperatures throughout the month, but starts a new graph when the first day of her next period arrives.

The temperature graphs of several months thus placed beneath one another allow an easy comparison of the cycles. The patient soon becomes familiar with the pattern of her menstrual cycles, and gross abnormalities will be easily discernible.

ANOVULATORY CYCLES

Physiologic anovulatory menstrual periods occur during adolescence and the climacteric. These can be studied by basal temperature graphs. After puberty the bleeding episodes occur at grossly irregular intervals which are not associated with ovulation. Maturity is heralded by ovulation, and at this time the menstrual cycles will usually assume a regular pattern. These changes are reflected in the basal temperature records.

The climacteric is associated with a progressive decline of ovarian function. Menstrual periods may come at increasingly prolonged intervals or may become grossly irregular. More and more of these bleeding episodes are anovulatory, and ovulation usually terminates long before menstruation completely ceases (Fig. 5).

OVARIAN FAILURE

Basal temperature recordings can be used to study ovarian failure. Minor degrees of failure may be associated with periods of amenorrhea, irregular bleeding, or both. The absence of ovulation can be

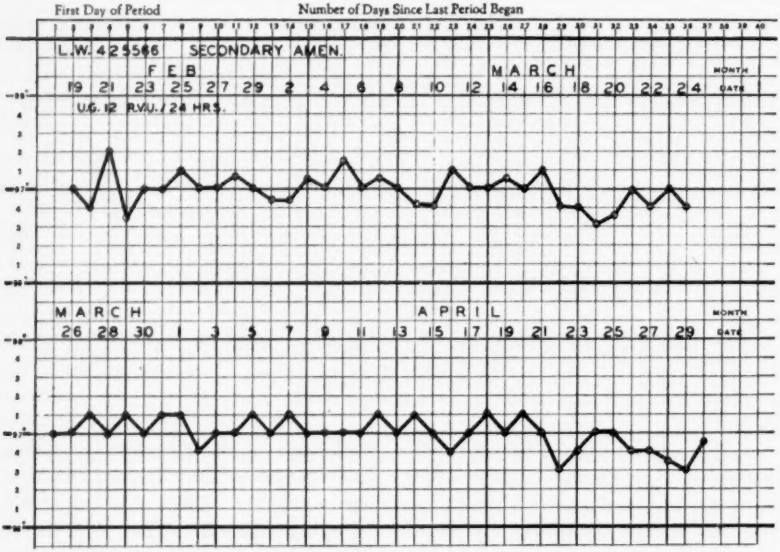

Fig. 6. Typical basal temperature graph of a young woman with ovarian failure and secondary amenorrhea. There are daily fluctuations in the temperature curve but no typical preovulation rise. Some follicle activity may occur in the ovaries but no ovulation or corpus luteum formation.

demonstrated in the graphs (Fig. 6). The temperatures will show minor fluctuations from day to day but will not exhibit the typical postovulatory elevation. If endocrine preparations are administered it is well to note them on the record in order to correlate their activity with basal temperature changes.

STERILITY

Basal temperature records provide pertinent information in the study and management of the infertile couple. The records serve to familiarize the woman with the normal physiologic changes which occur during the menstrual cycle and make her cognizant of abnormal variations. The record gives the physician information concerning the sex life of the couple.

The menstrual pattern is a good index of fertility. Regular periods usually are ovulatory. Grossly irregular periods are often anovulatory. The physician should review the graphs with the patient at each visit, giving her an opportunity to clarify any misapprehensions.

The fact that ovulation can be timed within twenty-four to seventy-two hours on the basal tem-

perature graph is extremely important if the husband has major sperm deficiency or if the couple has coitus at rare intervals only. As previously suggested, limiting sexual intercourse to the three or four days of the transitional period in the basal temperature record will increase the fertility of these couples (Fig. 7).

The record provides the earliest information of a possible gestation. If the temperature level remains elevated three or four days beyond the average length of the previous cycles, pregnancy can be suspected.

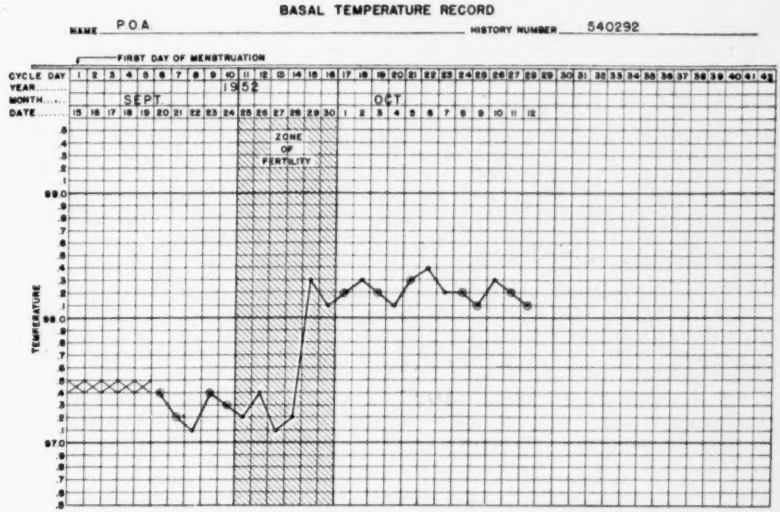

Fig. 7. Basal temperature graph of a typical cycle of patient P.O.A. The length of her cycles varies from twenty-seven to thirty-one days; they are thus of average length. Cycle-day 1, the onset of menstruation, was Sept. 15. She placed an x in the appropriate square under cycle-day 1 and noted the month and the day below this. She menstruated for five days and each morning placed an x under the cycle-days 1 through 5. On awakening on cycle-day 6, she took her temperature and recorded it promptly. She likewise circled this dot because she had intercourse the night before. The basal temperature continued at a low level until cycle-day 14 and it rose abruptly on cycle-day 15. This sudden rise was indicative of ovulation. She may have ovulated on day 13, 14, or 15. The temperature remained at its postovulatory elevated level for fourteen days until cycle-day 28, when she began to menstruate.

She did not wish to become pregnant and refrained from intercourse from cycle-day 11 through cycle-day 16, the zone of fertility. She then felt free to continue her sex life until the onset of the next period.

If this patient was an infertility problem, she would have been urged to concentrate her sex life during this zone of fertility, particularly on cycle-days 13, 14, and 15. If her husband had a sperm deficiency, intercourse would have been limited to this period.

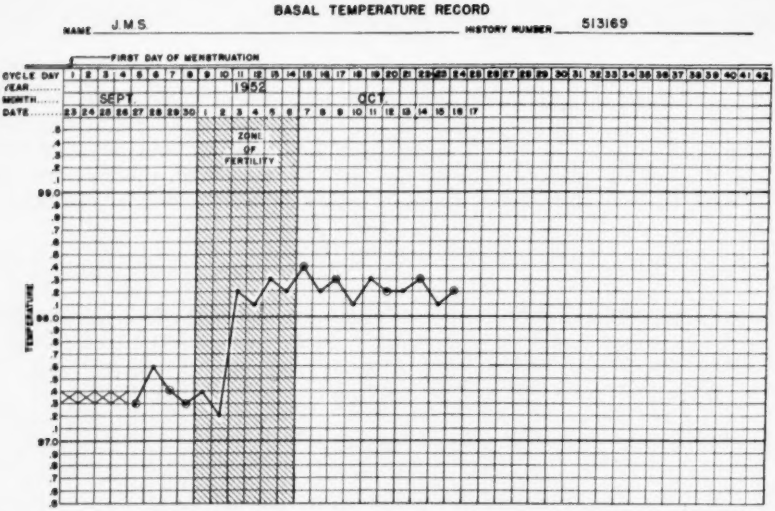

Fig. 8. Typical basal temperature graph of patient J.M.S. The pattern of her menstrual cycles differs from that illustrated in Figure 7 because they recur every twenty-four to twenty-five days. Note that the rise in body temperature from its low preovulatory level to its high postovulatory level occurred on cycle-days 10 and 11. This is the period of ovulation. In the use of this basal temperature graph for natural child spacing, the zone of fertility extends from cycle-day 9 through 14. This is the only method of child planning that this patient can use because of religious convictions.

The woman with a history of abortions should be instructed to refrain from coitus in these early days of gestation.

CHILD SPACING

Basal temperatures can be used to help interpret the periods of maximum and minimum fertility in normal women who wish to practice child spacing by natural means.

The individual who has established a normal basal temperature pattern may abstain from coitus during the transitory phase of the cycle when ovulation occurs. Thus, the married woman who has fairly regular menstrual cycles recurring every twenty-seven to thirty-one days can refrain from intercourse beginning with cycle-day 10 until day 16 or 17, when the temperature has reached the peak of its rise and has flattened out for at least forty-eight hours (Fig. 8).

¶ Although taking the basal body temperature over a period of a few months is undoubtedly a valuable mechanism for studying ovulation, it can be carried to the point where it loses practical value. The overanxious woman who lives by the thermometer is likely to concentrate so closely on temperature that the sex act loses its normal emotional quality, and the anxiety of "timed intercourse" may itself inhibit ovulation. Patients should be cautioned against living a "thermometered life."—A.I.W.

Prepared for Modern Medicine

Dating Ovulation by Endometrial Biopsy

ROBERT W. NOYES, M.D.,* ARTHUR T. HERTIG, M.D.,†
AND JOHN ROCK, M.D.‡
Harvard University, Boston

MICROSCOPIC examination of the endometrium yields useful information concerning time of ovulation and the degree of progesterone effect. Consequently, endometrial biopsy is a most valuable test for the physician to perform when confronted with a sterility problem.

By careful evaluation of the state of the endometrial glands and stroma, the experienced observer is often able to tell at about what time in the menstrual cycle ovulation occurred.

Numerous histologic variations take place in the endometrium as the menstrual cycle progresses. However, certain changes such as the degree of tortuosity of the endometrial glands and coiling of spiral arteries occur too gradually to be of value for dating purposes.

In general, morphologic progressions during the preovulatory or proliferative phase of the cycle permit recognition only of the early, middle, and late stages of proliferation. Day-to-day differences cannot be detected. The variable duration of the proliferative phase also hampers attempts to date ovulation by biopsy specimens taken before this event.

By contrast, endometrial changes during the postovulatory or secretory phase are more constant and sufficiently characteristic to permit arbitrary designation of day-to-day variations. We may speak of a secretory-phase biopsy as being taken on a certain postovulatory day, such as the second or the fifth. If one applies these dates to a classic twenty-eight-day cycle, assuming ovulation to occur on the fourteenth day, the second postovulatory day, for example, could also be referred to as the sixteenth day of the menstrual cycle.

Menses usually take up the first four days of a cycle. From the fourth to the eighth day the endometrium is thin, with narrow straight glands. The glandular epithelium is quite active, as evidenced by mitotic activity. The stroma is compact and the stromal cells appear to be mostly nucleus. Infrequent mitoses are seen.

By the tenth day the surface epithelium becomes tall and columnar. Slight tortuosity of the glands may be noted and some edema appears in the stroma. The endometrial gland epithelium shows many mitoses and has a pseudostratified appearance.

From the eleventh day until ovu-

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‡Clinical Professor of Gynecology, Harvard University.

lation the surface of the endometrium appears undulant and the glands tortuous; the stroma is dense, with many mitotic cells. Pseudostratification of glandular epithelium is marked.

After ovulation, no appreciable change in the microscopic appearance of the endometrium occurs for thirty-six to forty-eight hours. On the second postovulatory day, subnuclear vacuolization of the epithelium lining the endometrial glands appears—the first morphologic evidence of ovulation.

The vacuoles, which are large, clear, and regular, are due to early progesterone effect. In other respects the endometrium is quite similar to that seen during the proliferative phase. A few irregular vacuoles occasionally develop before ovulation; care must be taken to differentiate the two phases.

By the third postovulatory day the large vacuoles in the epithelial cells have pushed the nuclei toward the lumen of the glands. The result is a loss of much of the pseudostratified appearance. The glandular epithelium now appears layered with clear vacuoles lined up beneath the dark nuclei, which are separated from the gland lumen by homogeneous cytoplasm.

By the eighteenth day of a classic cycle, the fourth postovulatory day, the vacuoles become smaller, and some slip past the nuclei on their way to the lumen, where they will be discharged. The nuclei are in good alignment and no longer simulate stratified epithelium. Mitosis is absent.

By the fifth postovulatory day few vacuoles remain and the lumina of the glands contain shreds of secreted material which are visible in the stained section. One day later, glandular secretion is maximal and the shreds of material in the lumina are more compact and stain deeply.

The preceding descriptions reveal the importance of changes in the glandular elements of the endometrium in dating biopsies obtained during the first half of the secretory or postovulatory phase. The important histologic progressions during the last week of the menstrual cycle appear in the stroma.

On the seventh postovulatory day stromal edema is apparent and becomes marked by the eighth day. When edema is present the stromal cells appear as almost bare nuclei with only filamentous threads of cytoplasm connecting them. At this point, mention should be made of the ability of operative trauma to cause edema of the endometrium. This may be misleading at times.

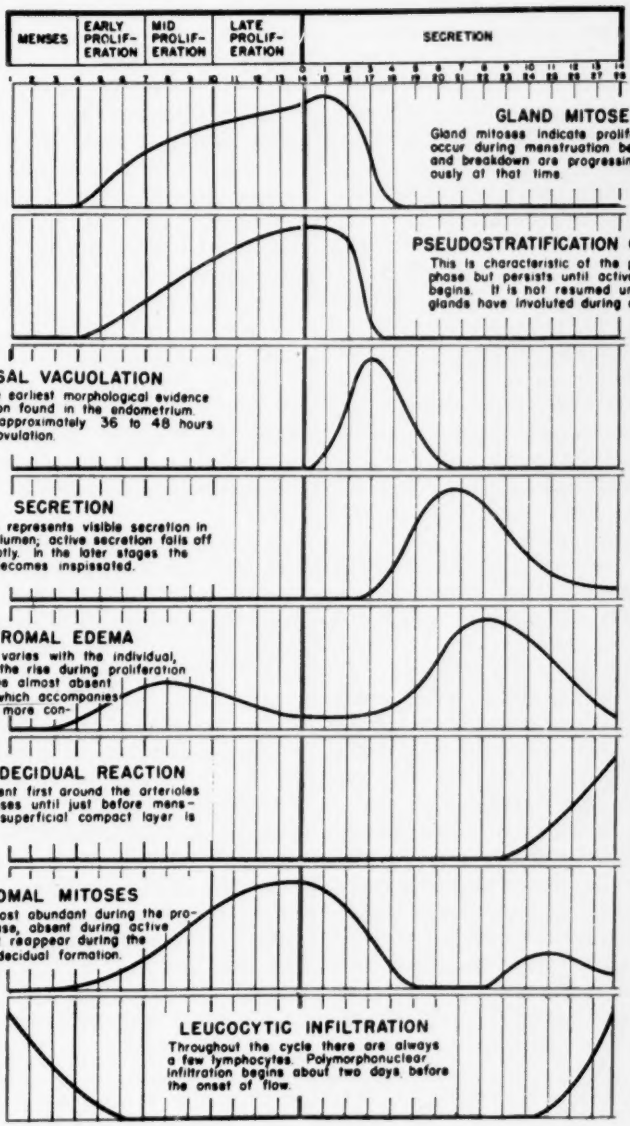
The twenty-third day of a classic cycle, postovulatory day 9, is distinguished by the rather sudden prominence of the spiral arteries. In biopsies taken earlier they are hard to identify.

Day 24 is characterized by definite collections of predecidual type cells formed from stromal cells near the arterioles. The stroma is active with mitoses while the glandular elements are involuting. The epithelial cells are low and ragged.

The following day a round-cell infiltration of the stroma becomes noticeable, and predecidual cells

DATING THE ENDOMETRIUM

APPROXIMATE RELATIONSHIP OF USEFUL MORPHOLOGICAL FACTORS



appear under the surface epithelium. By day 26, polymorphonuclear leukocytes are seen, and islands of predecidual cells form.

On day 27 the predecidua forms a solid sheet of well-defined cells, the endometrial glands are exhausted, ragged and flat in appearance, and leukocyte infiltration is marked. Microscopic areas of hemorrhage and necrosis herald the onset of menstruation within a few hours.

To summarize, the important changes during the first half of the secretory phase involve the epithelial cells and consist of mitosis, pseudostratification, basal vacuolization, and secretion. During the second part of this phase, important alterations occur in the stroma and include edema, predecidual reaction, mitotic activity, and leukocyte infiltration.

The accuracy of the biopsy method for dating ovulation was tested by examination of endometrial specimens from 300 normally menstruating women. In only 14% did menstruation begin on the day predicted from the biopsy. However, in an additional 24% it occurred within one day of the predicted date.

Most of the women menstruated before the predicted date. To test whether the biopsy itself hastened the onset of menses, biopsy dating was compared to the basal temperature change which occurs with ovulation. Ovulation day was arbitrarily taken to be represented by the low point on the curve which just preceded the sustained rise in basal temperature. By this criterion, 48% of the women ovulated on the date predicted by the biopsy study and an additional 31% within one day of the date.

The good correlation found between ovulation dated by temperature curve and ovulation dated by biopsy strongly suggests that the histologic criteria are accurate but that the biopsy maneuver hastens the subsequent menses, probably through injury to the endometrium. Further evidence is found in a study of menstrual period charts.

Biopsy often increases the number of days of bleeding in the subsequent menses, but rarely by more than two days. Later menses are then of normal duration.

For best dating results, special precautions should be taken in performing the endometrial biopsy and in preparation of the specimen. Biopsy specimens should be taken during the secretory phase, that is, after ovulation is considered to have occurred; those taken during the menses are of little use.

Tissue should be obtained from the fundus, and with a single firm sweep of the curet and should contain stratum compactum and spongiosum. It should be fixed immediately. Bouin's solution is well suited for this purpose. Careful dehydration, embedding, and staining are essential, and sectioning should insure vertical orientation.

Abnormal endometria cannot be accurately dated.

¶ This presentation is an abstract of a paper bearing the same title, originally published in *Fertility & Sterility* 1:3, 1950. The microscopic sections reproduced with the original are worthy of study. The reader who is particularly interested in dating the endometrial biopsy is referred to this paper.—A.I.W.

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What it does: The hypotensive action of *Rauwolfia serpentina* is of moderate intensity.[1] It is not apparent for several days after therapy is initiated and does not attain its maximum extent for weeks or even months.[2] When therapy is stopped, the hypotensive effect persists for some time.[3] Coincidentally with the hypotensive action, Rauwiloid produces a mild bradycardia, especially appreciated in the presence of the tachycardia which so frequently disturbs the hypertensive patient. A significant feature of Rauwiloid is the distinct sense of well-being and emotional calm it induces, as well as the prompt relief of symptoms experienced by the patient. In a series of 326 patients, drowsiness was noted in only seven.

The entire daily dose of Rauwiloid may be taken at one time, for instance upon retiring. Rauwiloid produces no undesirable side actions, even when given in excessive amounts. Dosage therefore is not critical, hence dosage calculation is not necessary. Rauwiloid is not a ganglionic or adrenergic blocking agent, and does not interfere with postural reflexes.

Available evidence shows that when a second hypotensive agent is given with *Rauwolfia serpentina*, its effect is exerted in addition to that of *Rauwolfia serpentina*.[1]

NOTE THESE ADVANTAGES

The desirable hypotensive action of Rauwiloid is characterized by these advantageous features. It produces

1. Pronounced subjective improvement
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4. No undesirable side actions
5. No toxic effects; there are no known contraindications

Indications: Rauwiloid is the medication of choice in mild and moderate hypertension; in severe and malignant hypertension its synergistic properties are valuably employed with other medication. There are no known contraindications.

Administration and Dosage: The initial dose of Rauwiloid is 4 mg. daily, given as a single dose at night, and continued until the desired effect has been attained. Maintenance dosage at 2 mg. daily can be instituted when symptomatic and objective improvement indicates, usually after one or two months.

How Supplied: Rauwiloid is available in 2 mg. tablets in bottles of 60, a month's supply of medication.

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The physician will appreciate the opportunity electively to lower the blood pressure without side actions with the aim of arresting the hypertensive process.

References:

1. Wilkins, R.W., and Judson, W.E.: The Use of Rauwolfia Serpentina in Hypertensive Patients, New England J. Med. *248*:48 (Jan. 8) 1953.
2. Wilkins, R.W.; Judson, W.E., and Stanton, J.R.: Preliminary Observations on Rauwolfia Serpentina in Hypertensive Patients, Proc. New England Cardiovas. Soc., 1951-1952, p. 34.
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Prepared for Modern Medicine

Reconstructive Fallopian Tube Surgery

B. BERNARD WEINSTEIN, M.D.*
Tulane University of Louisiana, New Orleans

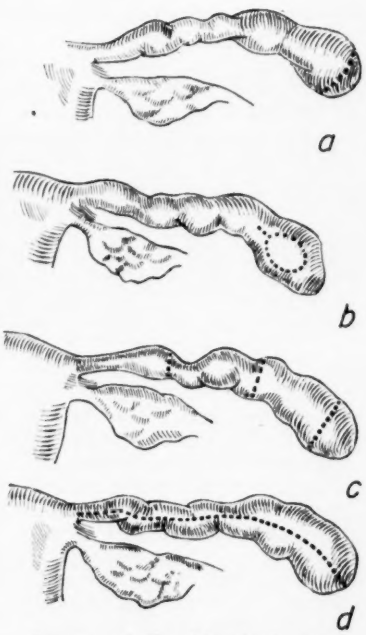
TUBAL obstruction or nonpatency, either partial or total, is the cause of sterility in approximately 50% of childless women.

As Rubin has pointed out, "at least ¼ to ⅓ of all women owe their childlessness to complete tubal obstruction, and . . . ¼ more suffer from some form of partial obstruction and peritubal adhesions or anomalous conditions." Thus the tubal factor is extremely important in sterility, and our attention is focused upon any therapeutic regimen that will increase ultimate tubal salvage and so enhance the potential fertility of these patients.

When tubal nonpatency is demonstrated by transuterine tubal gaseous (CO_2) insufflation and persists after repeated insufflations, the diagnosis is confirmed by hysterosalpingography, which also demonstrates the site of the obstruction. The patient should then be treated with all the conservative measures currently at our disposal. These include repeated insufflations at normal pressures, carefully controlled insufflations under increased pressures in selected cases, and pelvic diathermy, hormones, antibiotics, and chemotherapy.

With the combined use of various conservative procedures, discussed elsewhere in this Symposium, some degree of patency can be established in a varying percentage of patients with tubal obstruction. In our experience, approximately 42% of patients with a tubal factor have return of patency after

(Continued on page 132)



Courtesy of Dr. Eduardo Bunster, Trompia de Falopia, *Santiago, Chile.*

Fig. 1. Types of salpingostomy incisions: [*a*] terminal, [*b*] lateral, [*c*] transverse, and [*d*] linear

*From the Departments of Obstetrics and Gynecology, Tulane University School of Medicine, New Orleans.

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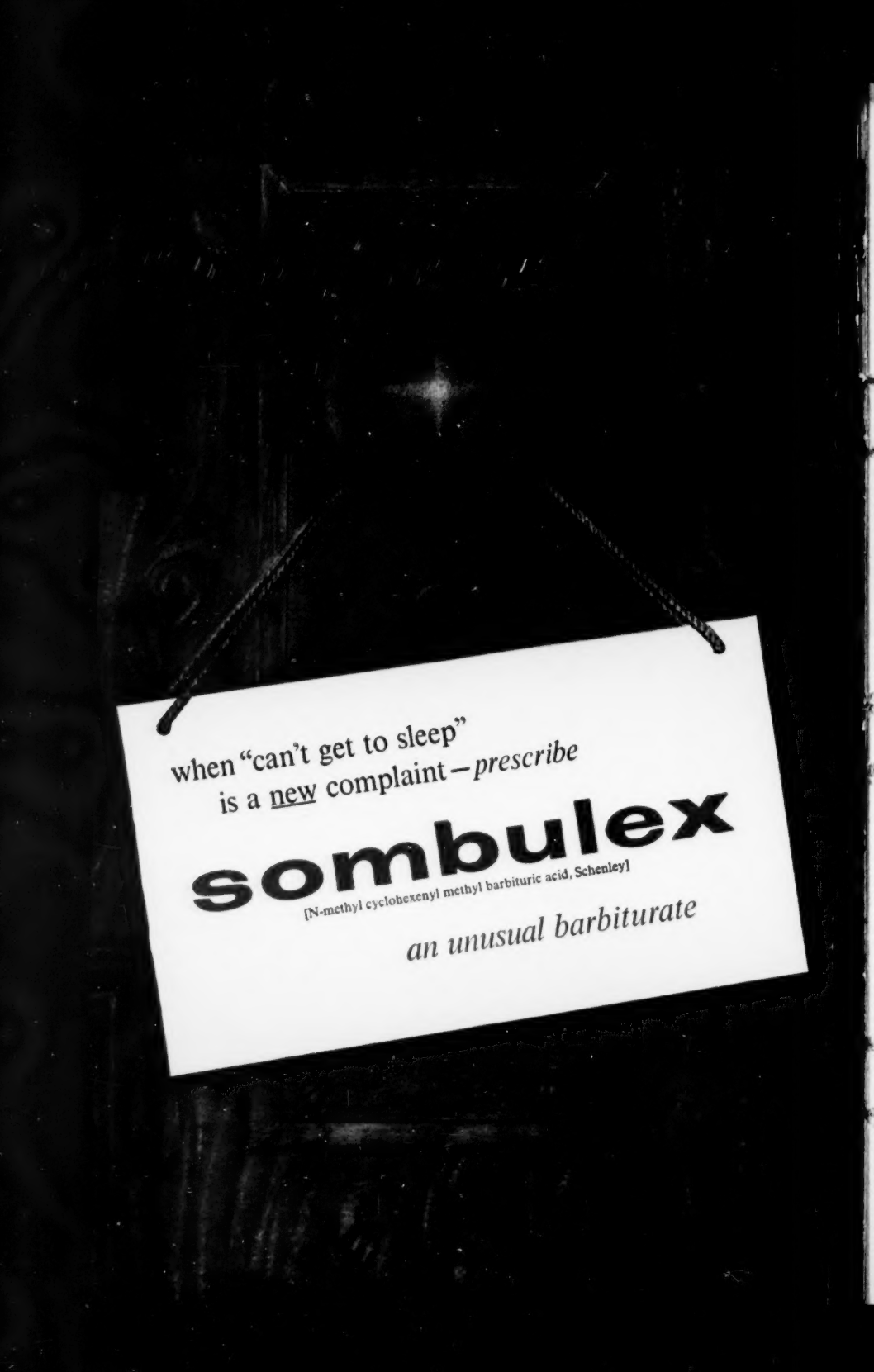
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such therapy and approximately 18% ultimately become pregnant.

There remains a group of patients, 58%, whose tubal obstruction persists despite all forms of conservative therapy continuously and conscientiously applied for over a year. It is from this group that we select our candidates for tubal surgery. However, certain requirements must be met:

- The couple must desire a baby very much.
- The husband must have a high fertility index.
- The wife should be well within the limits of the childbearing age.
- The wife must be free of systemic disease that would contraindicate surgery or pregnancy.
- Proof must be obtained by biopsy that the wife has a secretory endometrium (a normal basal temperature chart, and no endocrine dysfunction).
- The wife must be free of recent pelvic inflammation.
- The wife must have a low sedimentation rate which remains low after pelvic examinations.

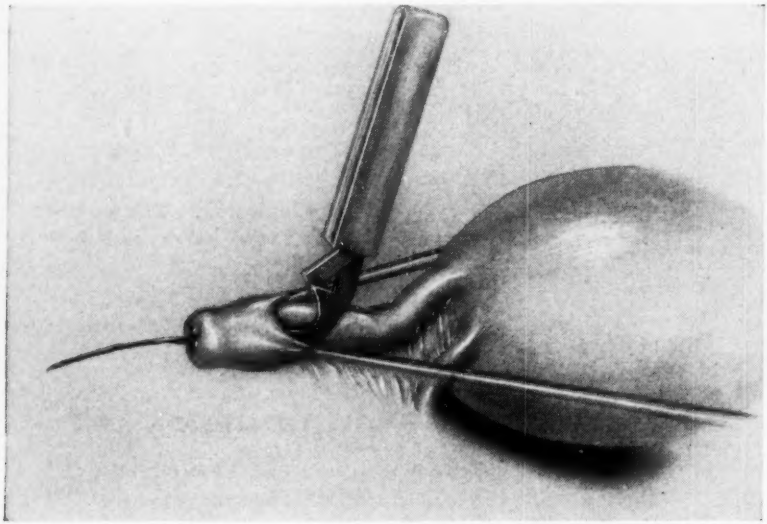

Fig. 2. Terminal salpingostomy. The cuff, once turned back, is sutured with 000 or 0000 chromic catgut or No. 120 cotton interrupted sutures.

- The wife should be a good surgical and *mental* risk.
- The couple should be informed of the possibilities involved in the procedure and the likelihood of failure. The possibility of failure in terms of tubal closure, failure to conceive, abortion, miscarriage, and ectopic pregnancy should be clearly explained. Honesty is essential if one is not to be plagued by one's conscience and by a group of greatly disheartened, discouraged, and hurt patients.

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*Oster, K. A., and Golden, M. J.: Exp. Med. & Surg., 7:37, 1949

...mild cases cured in one to two weeks treatment... moderate infections cured in two to four weeks... severe, long standing chronic cases cured within three months...

When these requirements are rigidly applied and met, the number of patients eligible for tubal surgery in any one clinical group should be small. We emphasize this point because we feel that *only a select group of tubal nonpatency patients should be subjected to surgery.*

Tubal surgery should be carefully and meticulously performed by a trained gynecologic surgeon, rather than by the occasional operator, if any degree of success is to be expected in these otherwise hopeless cases.

In addition to careful selection of patients, pre- and postoperative care must be adequate if tubal surgery is to be physiologically successful. *Tubal patency is not hard to restore, but is often difficult to maintain. Tubal physiology is extremely difficult to restore,* and not too often do we succeed. A patent tube does not necessarily mean a physiologically functioning tube. A patent tube need not mean a pregnancy. In our own series, approximately 88% of patients have maintained tubal patency for a year or longer after surgery, some 96% having shown initial tubal patency in the month or months immediately after surgery.

The patient should be prepared for surgery by administration of

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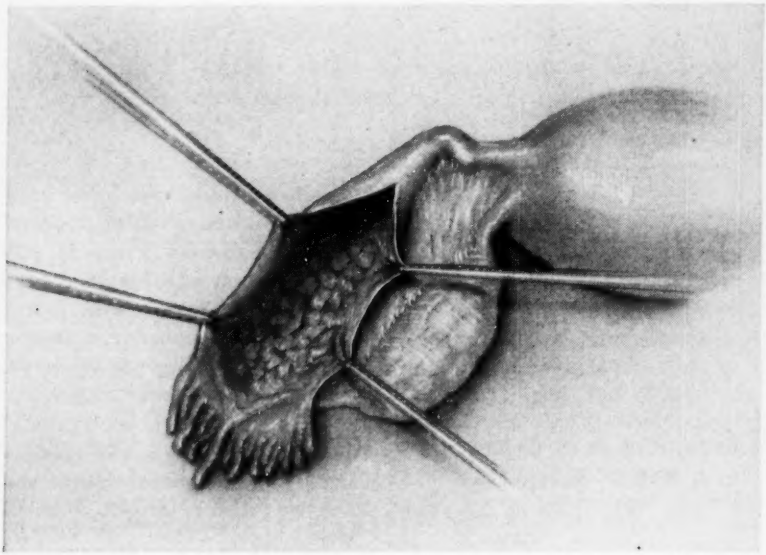

Courtesy of Dr. S. Leon Israel, Philadelphia.

Fig. 3. Linear salpingostomy. Tube is slit with sharp scissors, and fine-tipped hemostats are placed on bleeding points. Incision should be carried to cornu.

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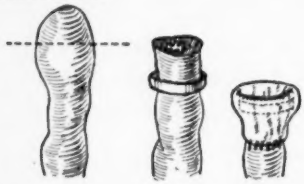
1. Reich, W. J., et al. (1952), A Recent Advance in Estrogenic Therapy. II. Amer. J. Obst. & Gynec., 64:174, July.

1-164

in Oral Estrogen therapy

hormones, antibiotics, or other medication when indicated, and by liberal application of diathermy. The immediate postoperative period should include such adjunctive therapy as is incidental to the surgery itself—maintenance of fluid and electrolyte balance and transfusion of blood, as well as repeated transuterine tubal gaseous insufflations when uterine tubal distenders are not used. If distenders are used, withdrawal should be followed by insufflations.



Courtesy of Dr. Edward Kahn and Fertility and Sterility, *Paul Hoeber Company, New York City.*

Fig. 4. Polyethylene ring used to maintain osteal patency in terminal salpingostomy

The surgical procedure will vary with the pathologic findings at laparotomy. It may consist of either lysis of adhesions or lysis combined with other surgical measures such as terminal, lateral, or linear salpingostomy, tubal resection and anastomosis, or tubal excision, resection, and reimplantation. Of the various procedures, lysis, terminal salpingostomy, and tubal reimplantation have given the best results.

The surgical technics vary slightly in any given case and vary considerably in the hands of different surgeons. In general, however, the following measures should prevail:

1] Careful selection of patients based upon the criteria listed above;

2] Careful preoperative preparation of the patient, including diathermy, hormones, antibiotics, and chemotherapy;

3] Careful preoperative preparation by the surgeon of his instruments and his team for tubal plastic operation. This includes the availability for use at the table of a transuterine tubal gaseous insufflating apparatus and some type of tubal distender, depending upon the surgeon's choice (polyethylene tubing, sugar sticks, Gelfoam sticks, catheters, and so on), and a group of special instruments including very fine silver probes, fine olive-tipped needles, small hemostats, delicate Allis clamps, cork borer, and the like;

4] At operation, absolute hemostasis; gentle handling of the tissues; adequate implantation so that the implanted tube ends do not slough; preservation of the tubal blood supply; demonstration of patency of the portion of the tube to be implanted; use of fine suture material, preferably atraumatic fine (000 or 0000) catgut or No. 120 cotton; and adequate openings in the fundus for implantation or in the tube for salpingostomy; and, finally

5] Particular attention postoperatively to the maintenance of tubal patency, in addition to routine postlaparotomy care. Liberal use of antibiotics and adequate follow-up are essential.

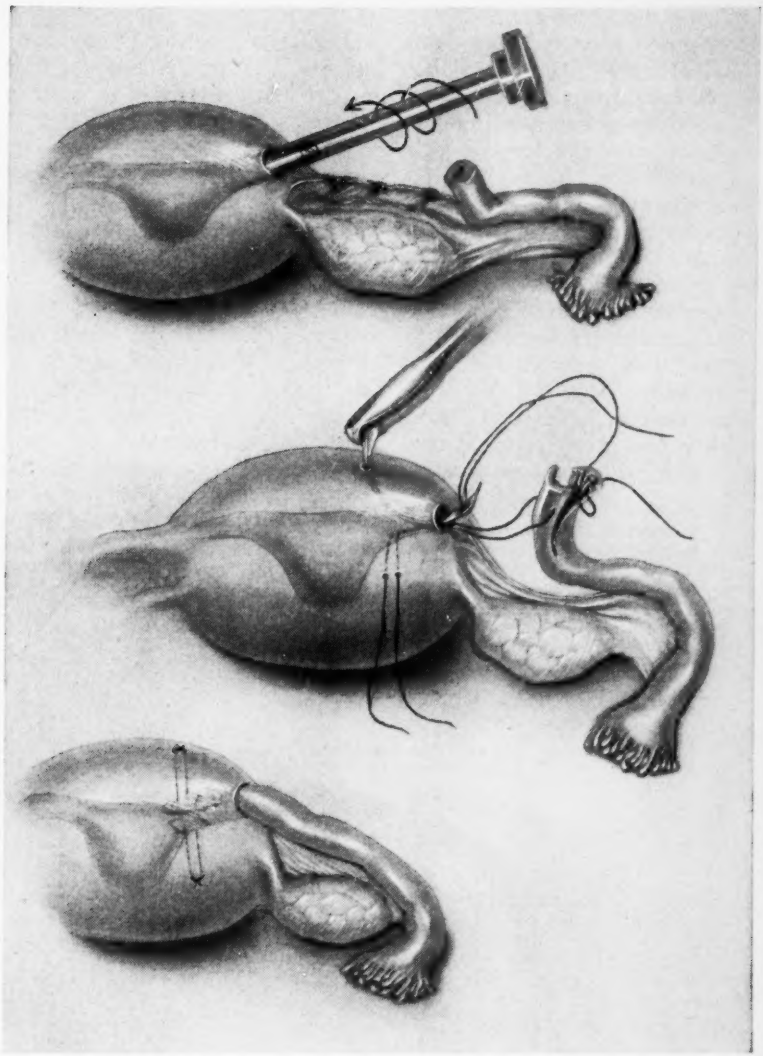


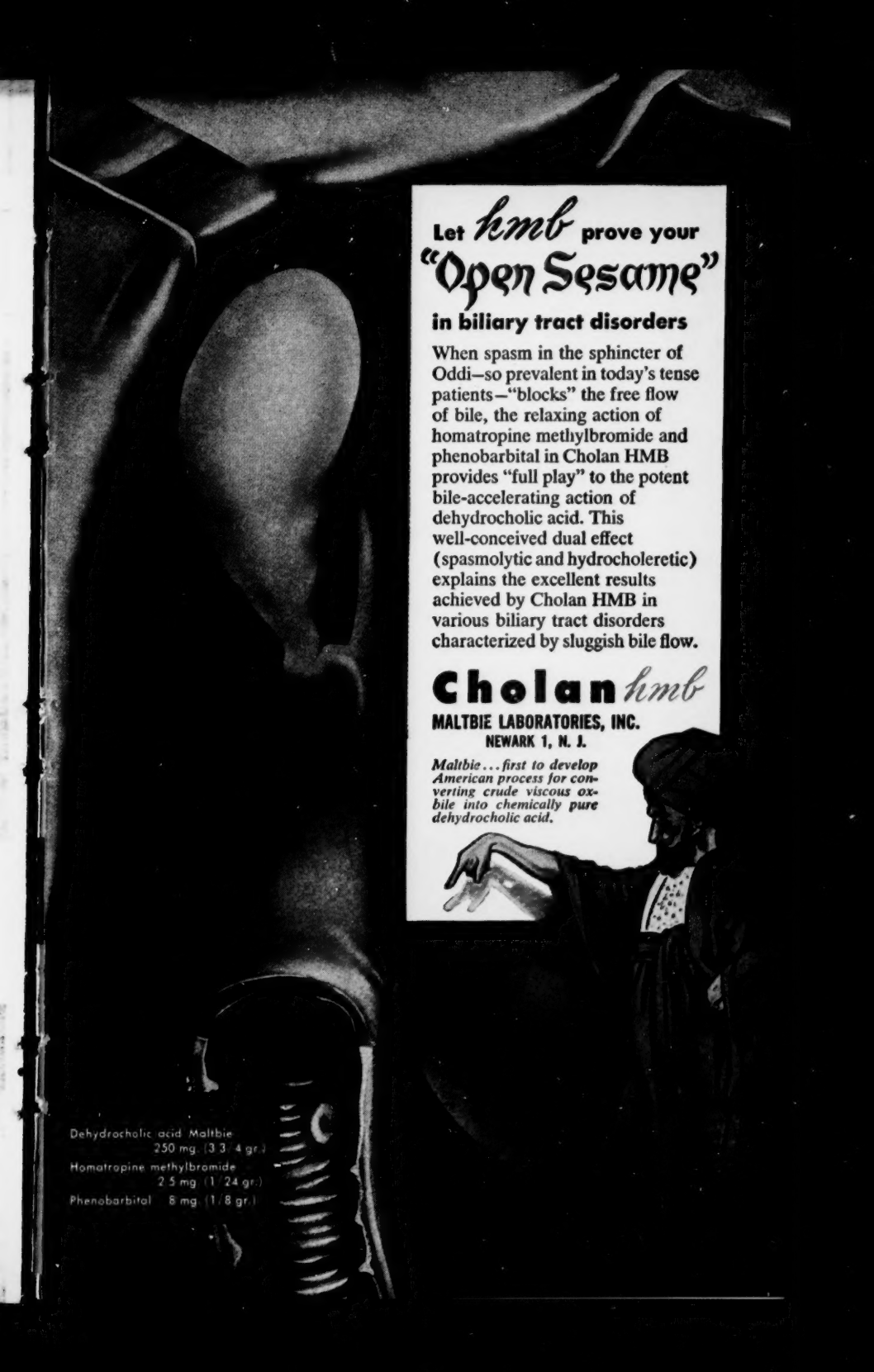
Fig. 5. Technic of tubal reimplantation. The coring may be done with a cork borer, as shown, or by wedge incision with a scalpel. Implantation may be made in an area immediately below the tubal stump or above in the fundal area. We have always excised the tubal stump and implanted in the resultant cornual area.

Utilizing the above methods, we have operated upon 109 women in a period of eleven years (1939-50). Postoperative patency has been maintained for one to three months in 96% of cases and for one year or longer in 88%. Among the 109 women there have been 49 pregnancies, 29 occurring among a group of 21 after salpingostomy. Also 1 ectopic pregnancy and 2 abortions have occurred.

These results are somewhat better than those reported for tubal surgery in the past, but still leave a great deal to be desired. However, it is our strong personal conviction that, with due consideration of the factors mentioned, an honest and diligent group of trained gynecologists can gradually improve the results of tubal plastic surgery, increase the percentage of successes represented by term pregnancies, and place operation upon the fallopian tube in its rightful place in the armamentarium of the gynecologist dealing with apparently hopeless cases of infertility.

The delicacy of the tissues involved has led us to advise those who plan to do tubal surgery for the first time to do some preliminary study upon human operative and cadaveric material and, when possible, upon the rhesus monkey.

¶ Achievement of 96% postoperative patency and 88% tubal patency after twelve months is unusual. The result of 49 pregnancies out of 109 patients subjected to surgery is quite startling. However, the author has constantly stressed the proper selection of the patient to be subjected to surgical intervention and there is no doubt that in selected cases the results are better than can be obtained at random. He has also constantly stressed the necessity for adequate preoperative preparation and postoperative follow-up. The author is to be congratulated on his insistence on proper selection. His results attest to his wise choice of patients.—A.I.W.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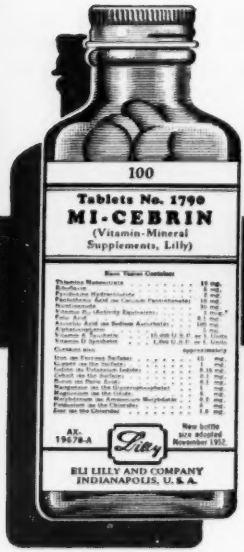

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General Therapy of the Female

ROBERT N. RUTHERFORD, M.D.*
University of Washington, Seattle

AS the concluding contributor to this Symposium on a new, yet increasingly promising field of study, I would like to suggest a relatively uncomplicated program of survey for the infertile female. For it is still the infertile *female* in the minds of our general population, although braver and braver statistical studies implicate the male partner with ever greater abandon. However, because the female organism is more complex, malfunction may be expected more frequently in the female than in the male.

MEASURABLE FACTORS

In any survey of the female, we must check upon:

• *Gross normality of internal and external genitalia.* This would exclude obvious genital abnormalities, infantilism, disturbances of position or of plane, infections, and the like. The need to correct such conditions is obvious and, in general, noncontroversial.

• *Proof of habitual ovulation.* This can be obtained by interpretation of basal body temperature charts or, more accurately, by microscopic interpretation of an endometrial biopsy specimen taken from high on the anterior or posterior uterine wall premenstrually or during the first few hours of menstrual flow.

Treatment of the patient who habitually fails to ovulate may be hormonal. There are myriad hormonal treatment patterns of varying scientific logic but of only fair success. If the patient's ovaries are not responsive to endocrine stimulation, one may have to resort to x-ray irradiation.

• *Proof of tubal patency and motility.* The classic Rubin test is still the general duty method to separate patients who deserve special study from those with normal tubal physiology. If the tubes fail upon 2 consecutive insufflations using carbon dioxide or a similar medium, disorder of tubal patency or physiology may be suspected.

Dyskinesia of the uterotubal valve has had a great deal of investigation. Agents aimed at relaxing this spasm are not universally accepted. Pressure methods from below have replaced surgery to a large extent and may be responsible for overcoming this physiologic spasm in many cases. Use of hormones has also been suggested.

In this type of spasm, the regular slough of tubal epithelium may be retarded, with inspissation of the retained material. Not only would this seem a common prob-

*Chief of Obstetrics, Virginia Mason Hospital; Clinical Instructor of Obstetrics and Gynecology, University of Washington, Seattle.

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lem, for many problems of tubal "closure" have no specific history of infection, but results suggest that pressure methods from below have relieved either valve spasm or inspissation in an unrecorded number of instances.

Studies of tubal peristaltic patterns have been useful at the investigative level but are difficult of interpretation. Treatment of impaired peristalsis presents a problem in many cases.

Direct visualization of the reproductive organs by peritoneoscope, culdoscope, or other methods is of interest but has not been applied generally except in working out problems of normal function. The allowable physiologic variations of the normal have still to be defined. These procedures cannot yet be applied therapeutically to replace pressure methods from below, posterior colpotomy, or exploratory laparotomy.

Surgical methods to relieve tubal occlusion or to repair damaged tubal physiology have been improving with the advent of antibiotics, more accurate diagnosis, earlier treatment, newer materials, and better physiologic knowledge on the part of the surgeon. The percentage of surgically treated cases is lessening each year because of earlier prophylactic treatment and better restorative nonsurgical methods. More will be said of this later.

• *Adequate function of the thyroid gland.* This fabled gland so capable of response to empirical treatment is under bombardment from all sides. By courtesy of the atom bomb, we now have radioactive iodine to aid in our investigation of this important adjunctive gland in the reproductive kaleidoscope.

Try to dislodge empiricism as we will, we still must admit that thyroid extract in dessicated form seems the most generally employed and most successful agent for treating the female who has a low fertility index but no other demonstrable physiologic problem. The general treatment plan for dessicated thyroid extract is to carry the patient's metabolism slightly above its normal level. The basal metabolic rate is a crude test, but despite the introduction of the iodine uptake test, determination of the serum protein-bound iodine, and other more exact determinations, it still is a useful tool.

Thyroid confounds us by giving good results for many patients who have no other demonstrable inadequacies (and for their male partners, too). The incrimination of this gland in the feminine "fatigue syndrome," in hypogenitalism, and in other general metabolic diseases in which the fertility index of the individual is low, would suggest that we are here on the verge of exact and useful knowledge.

• *Assurance of no obstetric hazard.* The couple should be evaluated medically as to health and possible obstetric peril for the woman. There is the story of the mythical specialist who treated his patient for sterility—she became pregnant before he made his first blood pressure test; then her nephritis required interruption of the pregnancy! An over-all medical survey is imperative.

ESOTERIC FACTORS

• The psychogenic factors in infertility seem to hover in the hypothalamic areas of the brain, the so-called "survival brain," or emergency unconscious levels. The single common denominator is yet to be proved, but from many sources we can reasonably infer the following:

1] Successful impregnation does not require complete sexual satisfaction on the part of the female.

2] Too great focus of attention upon the ovulatory mechanisms may interfere with ovulation, whether this interference be mediated through thyroid imbalance or through higher center confusions.

3] When the experimental animal is painfully stimulated at the time of mating, the role of the cervix or the uterus in aiding sperm passage into the tubes may be inhibited or impaired beyond the life span of the ovum.

We have all been confronted by the couple who have had all measurable factors studied and corrected. They fail to conceive until they abandon further efforts, adopt a child, or in a similar way release their tension control centers—only to conceive with benefit of clergy but without medical credit.

Early in our work, it became apparent that focusing the couple's attention upon body temperature change was of doubtful judgment. The husband often resented such regimentation. The wife frequently became functionally unresponsive and a passive receptacle.

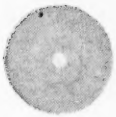
On the other hand, since ovulation varies somewhat and sperm are recoverable in the uterus and tubes for some fifty hours after implantation, it seemed wiser to plan a seven- or eight-day phase each month as a "fertile phase." During this period, because the male requires about forty-eight hours to recreate an effective sperm charge, the husband is requested to leave a fresh supply in his female partner every other day during this seven- to eight-day phase, calculated as some eighteen through ten days before flow is expected.

This measure anticipates the usual physiologic variations of the female cycle and provides a fresh supply of sperm during this phase as a "relative commitment" on the part of the male partner. This simple explanation seems of value for the infertile couple under pressure from outside informational sources.

• Habits of intercourse are as varied as human imagination. In general, much to the husband's relief, we suggest the above pattern of fertile phase. In other words, a fresh supply of sperm is planned on a forty-eight-hour cycle, but the husband donor is not committed to a training schedule as religious as that of the prize fighter.

General hygienic methods seem adequate. Too frequent exposures of the wife or too timed or too dedicated exposures have a negative effect on both members of the team.

The couple are definitely told that after the basal body temperature chart has been used to establish the fact that the wife ovulates habitually, the chart should be used as a check once every three or four months, not as a constant daily preoccupation.



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• Both partners must be warned that impregnation is not a simple matter like ordering a malted milk from the nearest drugstore. Our own figures suggest that it takes an average of six to seven months for the ordinary couple to effect a pregnancy. In the timed-exposure, preconceptionally-primed-with-hormone couple, this interval may be lessened unless each or both are under great tension. Our usual statement to the patients is that we expect a year in which to accomplish results and that it is our role to do the professional worrying. Only in this fashion can we be certain that the patients' normal physiology will persist.

• Not infrequently we are met with the fact that the drive to conceive represents an abnormal compulsion on the part of the female. Often this woman is a poor sexual partner who feels that she must conceive in order to prove that she is at least that much of a woman. This functional tension in the wife, the resistances in the husband, and the poor environment into which their symbol-child will be brought add up to a very real and common problem. These patients must have a different kind of corrective treatment before conceiving a child.

THERAPY PROGRAMS

The need for complete medical as well as physiologic and psychologic evaluation of the couple has already been stressed. Reassurance must be added, plus the assumption of responsibility and strain by the professional adviser.

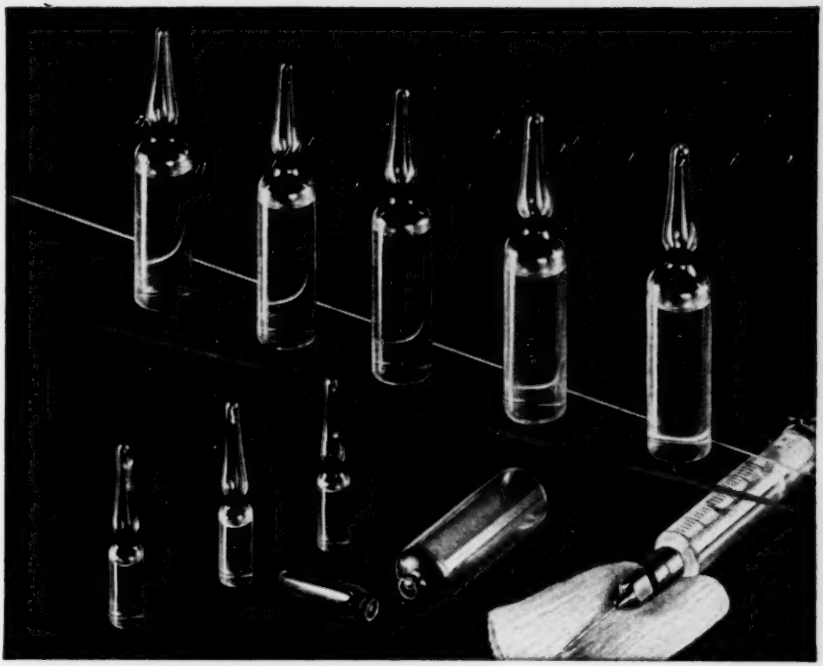
Certain medications as well as calendar activities may be of value:

• Thyroid still is used empirically with success. Roughly speaking, even if the patient's thyroid function is within normal limits, small amounts of dessicated thyroid extract may be of value. The basal metabolic rate should be corrected to roughly plus 5. Scientific proof of this contention still has to be accepted widely.

• Small doses of estrogenic substances may help. It has been suggested that using 0.5 mg. of diethylstilbestrol from the end of one flow to the start of the next may help in two ways. Penetration of the cervical mucous plug by the sperm may be aided, thus avoiding consideration of cervical mucus-sperm incompatibilities and of "sperm-encouraging" nutritive douches. Also, a better proliferative phase of the endometrium may be given, possibly aiding a more successful nidation of the fertilized ovum, with less chance of spontaneous abortion.

Stilbestrol is still the "poor man's progesterone," but either progesterone or biologically occurring estrogens may be used. Price is a real factor.

In honesty, it must be reiterated that any group observed preconceptionally will do better than any random-chance romance group will, either in achieving pregnancy or in lowering the pregnancy-discard rate. It has been estimated that one may achieve 60% success in any group upon which is lavished simply benevolent care and no medication. We cannot as yet evaluate the role of the one or the other, but



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these so-called priming routines seem to be of value.

- Timing of exposures to pregnancy and frequency of intercourse should be emphasized.
- Relaxation on the part of the couple is important.

THERAPY AFTER FAILURE

After failure in one calendar year, one may review the prognosis with the couple.

Reparative surgery may be of value either in the occlusive tubal cases or when partial resection of the ovary may relieve habitual anovulation. The couple should be briefed fully in the statistics of the situation, but should not be denied this final recourse, after full consideration.

With the advent of nonirritative tubing over which to reconstruct damaged tubes, with antibiotics, and with earlier surgery, the figures of salvage in this progressively smaller group continue to improve. The use of adjunctive routines, such as pelvic diathermy or antibiotics in the chronic inflammatory problem (either extra- or intrapelvic nidus), has not been endorsed widely or consistently. Implantation of the ovary into the uterine wall is hard to defend. The percentage of success is minute.

One owes it to the couple to take inventory of the situation at regular intervals, and if unsuccessful after conscientious scrutiny and effort, ought to recommend either adoption or a reevaluation of the case by another physician. Above all, it is a shared problem of the infertile *couple,* not an infertile wife or husband. Our scientific detachment regarding this reproductive problem should not disfigure an otherwise satisfactory marriage. There is considerable future for applied research in this still speculative field.

¶ In this short paper the author has presented an excellent survey of the general treatment of the infertile female. However, the editor feels that pituitary and ovarian x-ray irradiation should be stressed, since it has recently been shown to be one of the best methods of treating the anovulatory patient. Despite the ill effects of gamma radiation of Drosophila, fruit flies, the consensus regarding possible chromosomal mutations in the human being is that the risk of possible third-generation mutation is well worth taking in order to relieve barrenness. In the hands of an experienced radiotherapist, pituitary and ovarian irradiation is today an accepted and valuable means of inducing ovulation in the nonovulating woman.—A.I.W.

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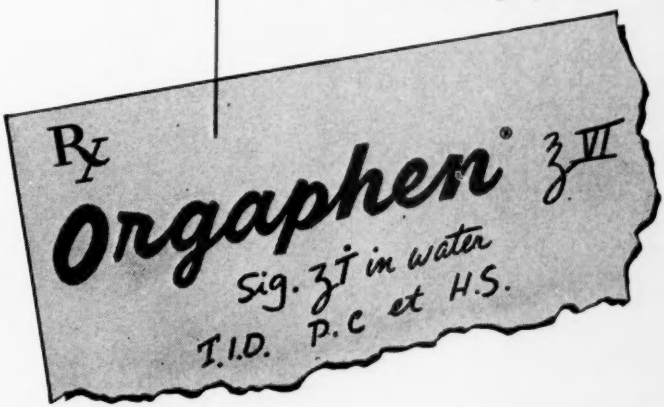

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Am. J. Med. *4*:875, 1948. Slaughter, Donald; Grover, Wm. C., and Hawkins, Richard. Report to American Therapeutic Society, Boston, 1950.

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A 2-drug regimen is effective for control of malaria brought back from Korea by returning soldiers.

Primaquine for Vivax Malaria

REPORT TO THE AMA COUNCIL ON PHARMACY AND CHEMISTRY

MOST cases of Korean vivax malaria can be terminated by a combination of chloroquine and primaquine. Standard dosage is safe enough for large scale treatment, even under the limited medical supervision available on troop transport vessels.

Acute attacks are suppressed by 1.5 gm. of chloroquine base. During the first twenty-four hours, 3 doses of 0.3 gm. each are taken orally, then 0.3 gm. daily in single doses for two days.

Relapse is prevented by primaquine, which destroys the parasite in body tissues. Daily doses containing 15 mg. of base are started with chloroquine and given for fourteen consecutive days. The regimen must be followed strictly. Though less dangerous than pamaquine, primaquine is potentially toxic, and large amounts may cause hemolysis, especially in Negroes.

Mass therapy in subclinical cases is described by Alf S. Alving, M.D., of Chicago and Maj. John Arnold and Maj. Donald H. Robinson, M.C., U.S.A.

When American forces entered Korea in the summer of 1950, unexpectedly heavy malarial infection developed, and chloroquine was administered routinely. The illness was of the temperate zone type, with a latent period of six to nine months between first and second attacks.

Troops returning home in 1951 discontinued medication, and relapse rates eventually exceeded 600 a week. Trials of primaquine, an 8-aminoquinoline related to pamaquine, were made under actual conditions of military rotation.

Standard doses of primaquine were given for twelve days to 742 men aboard a vessel sailing from Japan to Seattle, while 751 received a placebo. A second group of 2,060 men took 2 to 10 pills before embarking and continued the therapy on shipboard, while 725 others were given placebos. No sign of toxicity occurred, and seasickness was no more frequent during therapy.

The Armed Forces therefore adopted primaquine for all servicemen returning from Korea. The project was endorsed by the Subcommittee on Malaria of the National Research Council and the Armed Forces Medical Policy Council.

Comparison of primaquine and pamaquine was made, as reported by Capt. Paul L. Garrison, Lt. Daniel D. Hankey, Capt. Walter

Status of primaquine. 1. Mass therapy of subclinical vivax malaria with primaquine. 2. Cure of Korean vivax malaria with pamaquine and primaquine. 3. Toxicity of primaquine in Caucasians. 4. Toxicity of primaquine in Negroes. J.A.M.A. 149:1558-1570, 1952.

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G. Coker, Lt. Col. William N. Donovan, and Col. Bruno Jastremski, M.C., U. S. A., G. Robert Coatney, U. S. Public Health Service, Washington, D. C., Alf S. Alving, M.D., of Chicago, and Ralph Jones, Jr., M.D., of Philadelphia.

Malarial recurrence was tabulated for 709 veterans observed for four to eleven months after treatment in station hospitals.

Of 232 patients given chloroquine alone, 27.6% had at least 1 subsequent attack. Of 246 who took chloroquine and 27 mg. of pamaquine daily for two weeks, 1, or 0.4%, relapsed. Neither recurrence nor toxicity was noted among 231 subjects receiving the standard course of chloroquine and primaquine.

Primaquine toxicity in Caucasians was investigated by Capt. Charles B. Clayman, Maj. John Arnold, Capt. Robert S. Hockwald, Capt. Ernest J. Yount, Jr., and Capt. John H. Edgcomb, M.C., U.S.A., and Alf S. Alving, M.D.

From 10 to 240 mg. per day was administered to 699 white adults. Results showed that dosages of 15 mg. may be safely given daily for two weeks without special medical supervision. Daily doses of 30 mg. appear feasible for ambulant white subjects under observation, but hospital regulation seems necessary for larger quantities or treatment during disorders involving blood or bone marrow.

Weekly and semiweekly doses of 30 mg. taken by 50 adults for as long as fifty-two weeks did not cause serious reactions when used in combination with 0.3 gm. of chloroquine.

Primaquine toxicity in Negroes was investigated by Capt. Robert S. Hockwald, Maj. John Arnold, and Capt. Charles B. Clayman, M.C., U.S.A., and Alf S. Alving, M.D., who report that doses of 30 mg. involve definite risk of hemolytic reaction among deeply pigmented races. However, the standard dosage of 15 mg. of base for two weeks is apparently harmless.

Although subjective complaints were negligible, severe progressive anemia developed in 5 of 110 volunteers given 30 mg. of base daily. This anemia was of the same degree produced by 30 mg. of pamaquine base daily.

¶ POSTOPERATIVE MYXEDEMA develops most frequently by the end of the third month in hyperthyroid patients treated preoperatively with antithyroid drugs. Elmer C. Bartels, M.D., of the Lahey Clinic, Boston, finds the condition 5 times as often after primary hyperthyroidism as after adenomatous goiter and twice as often in persons subjected to a second operation. Hypothyroidism occurring in 69 of 942 thyroidectomized subjects was permanent in 49. Strumitis was 6 times as frequent as in the nonmyxedematous group. All myxedematous individuals were given dessicated thyroid. The smallest daily dose required was ⅛ gr.; the largest, 2 gr.
J. Clin. Endocrinol. & Metabol. 13:95-106, 1953.

Gold salts have not been replaced as the most valuable treatment for rheumatoid arthritis.

Medications for Rheumatoid Arthritis

JOHN LANSBURY, M.D.
Temple University, Philadelphia

AT least 30 drugs, many of recent origin, exert some favorable effect on rheumatoid arthritis. However, most of these medications are either too weak or too unpredictable to be of value or may cause serious side effects.

In discussing agents of merit, John Lansbury, M.D., observes that none replaces a program of rest, physical therapy, and the usual symptomatic and supportive measures.

The *salicylates,* which have excellent pain-relieving properties, should be used in all cases of rheumatoid arthritis on a regularly prescribed dosage schedule. Taking 15 gr. of acetylsalicylic acid on awakening, fifteen minutes before getting up, will often aid the problem of early morning stiffness. During the day 5 to 10 gr. can be ingested every four hours.

Butazolidin has approximately 8 times the analgesic action of the salicylates. The average dose is 100 mg. two or three times a day, but discomfort returns promptly when the drug is withdrawn.

Undesirable side effects such as anorexia, nausea, bloating, pain resembling that with peptic ulcer, gastric hemorrhage, morbiliform skin rashes, anemia, and leukopenia occur in about one-fourth of patients receiving Butazolidin. Therefore, the drug should be given only when the risk is justified, and serial blood counts should be made to detect leukopenia and bone marrow suppression.

Gold salts are still the most valuable agents in the management of rheumatoid arthritis if properly used. Gold therapy is worth a trial in all but the far advanced ankylosed cases but is not effective in rheumatoid spondylitis and should not be given to patients with liver or kidney disease or low leukocyte and platelet counts.

The patient receives, on successive days, 1, 3, 6, and 15 mg. of sodium aurothiosulfate in 1 cc. of sterile water intramuscularly. After this test dose the patient is examined for signs of intoxication; a white blood count, a differential count, and urinalysis are made.

If no untoward results are found, 25 mg. is given intramuscularly twice weekly for six weeks. Once a week the blood counts and urinalysis are repeated, and before each injection of gold the patient is questioned about itching, skin rashes, sore gums, diarrhea, and polyuria.

The place of drugs in the treatment of rheumatoid arthritis. Delaware State M. J. 25:29-34, 1953.

IN ANY ALLERGY

'Co-Pyronil' *

affords

more profound,

more prolonged

relief with

fewer side-effects

than any other

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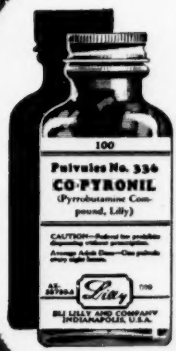
antihistaminic.



*'Co-Pyronil' (Pyrrobutamine Compound, Lilly)

Dosage

Mild symptoms: 1 pulvule every twelve hours.

Moderate symptoms: 1 pulvule every eight hours.

Severe symptoms: 2 pulvules every eight hours.

Lilly

If no signs of intoxication exist, 25 mg. of gold salts is given once per week indefinitely.

If remission is complete after 1,000 mg. has been injected, the dosage may be tapered gradually until 25 mg. is given intramuscularly only once a month. Twice weekly injections should be started promptly if relapse occurs.

BAL, cortisone, and ACTH are effective for treating toxic complications arising during gold treatment.

The frequent complications attending prolonged use of high doses limit the value of *ACTH* and *cortisone*. These agents should be used only when all other measures have failed and the patient is rapidly getting worse.

The smallest dosage adequate to give a reasonable degree of relief should be sought. Small doses are employed originally and gradually increased to a level of not more than 50 or 65 mg. of cortisone or 15 to 20 mg. of ACTH daily. If large original doses are given, the patient will be forever trying to recapture the temporary euphoria and pain-free state first obtained.

Physiotherapy and other rehabilitative measures must be employed simultaneously.

Very small doses of cortisone, 10 to 25 mg. daily, may be used in depleted cases to improve appetite and nutrition and, occasionally, at the beginning of a course of gold therapy before the gold effect is established.

During administration of the steroids, salt intake should be restricted and infections carefully watched for and promptly treated. When the drug is to be discontinued, the effect should be tapered with diminishing doses of ACTH.

ACTH and cortisone are not given to the aged, the mentally unstable, or menopausal patients or to patients with hypertensive cardiovascular disease, peptic ulcer, or tuberculosis of the lungs. These agents are also avoided in pediatric cases if possible.

Compound F, *hydrocortisone*, is particularly useful when injected locally into joints in 25- to 37.5-mg. amounts.

When an infectious element is associated with rheumatoid arthritis, the employment of *antibiotics*, especially terramycin, may be efficacious occasionally.

¶ CHOLANGIOGRAPHY yields diagnostically superior films when an aqueous emulsion of ethyl iodophenylundecylate is used as the radiopaque material. In both preoperative and postoperative radiography the advantages ascribed to this medium by Everett L. Pirkey, M.D., Lawrence A. Davis, M.D., and Lawrence A. Pilla, M.D., of the University of Louisville are lower viscosity and surface tension, better penetration of the smaller ducts, and lack of droplet formation. Because the substance is not absorbed through the walls, delayed studies are possible.

J.A.M.A. 151:266-268, 1953.

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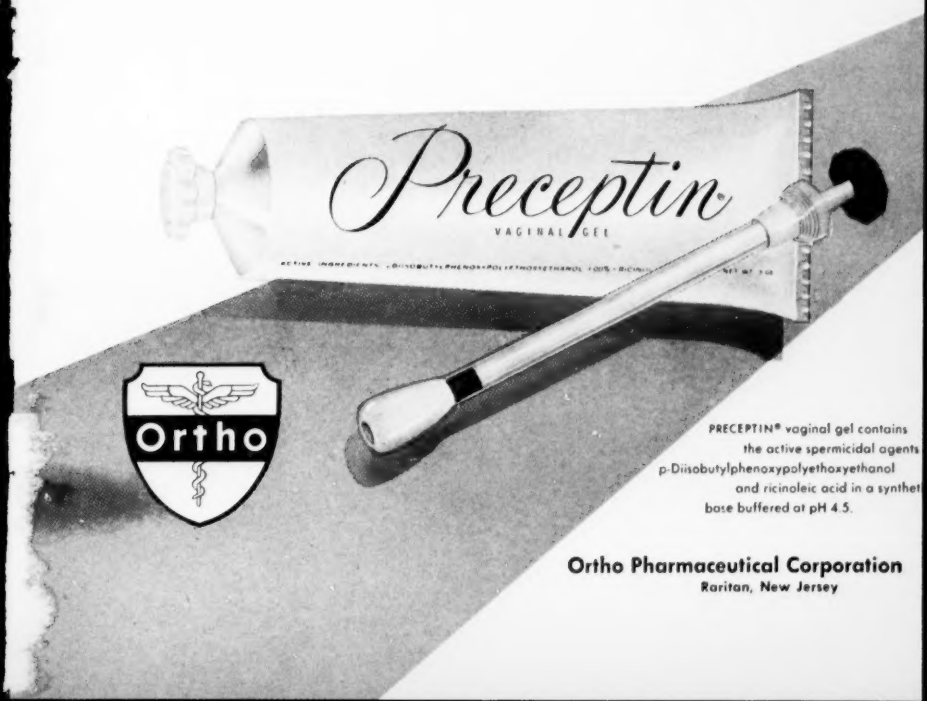


PRECEPTIN® vaginal gel contains the active spermicidal agents p-Diisobutylphenoxypolyethoxyethanol and ricinoleic acid in a synthet base buffered at pH 4.5.

Ortho Pharmaceutical Corporation
Raritan, New Jersey

Trichloroethylene anesthesia or analgesia is safe, convenient, and suitable for many common procedures.

Status of Trichloroethylene

MAX S. SADOVE, M.D., GORDON M. WYANT, M.D., AND LLOYD A. GITTELSON, M.D.

University of Illinois, Chicago, and Veterans Administration Hospital, Hines, Ill.

RELATIVELY new in the United States, trichloroethylene has been widely used in Great Britain. The agent has great possibilities, particularly as an analgesic in office practice, when use of general anesthesia is difficult or hazardous. The easily portable inhaler makes employment for emergency conditions outside the office also practicable.

Trichloroethylene is noninflammable when mixed with air at room temperature. Induction and recovery are rapid and postoperative nausea and vomiting are rare. Bleeding and salivation are not increased.

Among the great variety of uses for trichloroethylene as an analgesic agent, Max S. Sadove, M.D., Gordon M. Wyant, M.D., and Lloyd A. Gittelson, M.D., cite relief of pain during the first stage of labor; changing of painful dressings; incision of thrombosed hemorrhoids; myringotomy, cystoscopy, and other endoscopic procedures; painful examinations; suture of small and superficial lacerations; manipulation of minor fractures; dental and minor surgical procedures. The compound may be used as a supplement to local and spinal anesthesia, if epinephrine and similar drugs are avoided.

Technic for analgesia—A trichloroethylene-air mixture is usually administered by a special inhaler, such as the Cyprane or Duke inhaler, the open drop technic being difficult and hazardous because of the low volatility of the drug. In most of the special inhalers, the amount of air passing over the surface of the drug is regulated by a dial so that the remaining air is by-passed directly to the patient.

The dial may be locked in place at the position satisfactory for analgesia for a particular patient. Thus analgesia may be self-administered by the patient, who cannot alter the concentration of the agent. Should anesthesia supervene, the inhaler will slip from the patient's grasp, only air will be breathed, and consciousness is rapidly regained.

No rebreathing occurs, so accumulation of carbon dioxide is avoided. Since air is being drawn over the analgesic agent, hypoxic concentrations are prevented.

General anesthesia—The closed circuit technic cannot be used since

Trichloroethylene in general practice. Illinois M. J. 103:95-101, 1953.

trichloroethylene reacts with the soda lime of the carbon dioxide absorption unit. This necessitates adaptation of most anesthetic machines to a nonrebreathing system.

Trichloroethylene is hardly ever used as the sole anesthetic agent but rather as an adjuvant, particularly to nitrous oxide. Use of small amounts, 0.5 to 1%, enables maintenance of nitrous oxide anesthesia with 30 and even up to 50% oxygen, thus removing the threat of hypoxia from nitrous-oxide anesthesia.

Excessive doses of trichloroethylene may cause tachypnea and tachycardia.

Chronic Laryngeal Stenosis in Children

ROBERTO MACHADO, M.D.

DILATATION of the larynx with rubber Nélaton catheters reduces hospitalization time and brings rapid improvement for children with chronic laryngeal stenosis. Each bougie is left in place for a week, when a larger one is substituted.

Roberto Machado, M.D., of the Municipal Children's Hospital, Havana, reports complete recovery of 3 patients treated by the procedure, termed permanent retrograde progressive dilatation of the larynx. For children, the method is preferable to surgery because the laryngeal cartilages are growing and can be molded. A good laryngeal patency and voice are obtained.

Dilatation is done with regular rubber Nélaton bougies from 6 to 20F. Using direct laryngoscopy, dental floss is threaded through the stenosis and brought out the tracheal stoma. In case of complete atresia, a laryngeal needle or knife is employed.

The bougie, lubricated with K-Y jelly, is then inserted into the tracheal stoma and an end is attached to the leading thread. The bougie is pulled up through the larynx and pharynx and out through one nasal fossa. The end that goes through the nostril is left loose, the other is anchored to the tracheal cannula.

Each week the bougie is replaced by the next larger size until the desired dilatation is obtained. The last size is replaced for three consecutive weeks, then entirely removed, and decannulation is started by the regular procedures. The tracheal stoma is closed by reconstructive surgery.

The bougie is well tolerated, and patients have no difficulty in swallowing food. A slight increase in mucus in the nostril containing the catheter is controlled by instillation of sodium chloride bicarbonate solution.

Permanent retrograde progressive dilatation. Arch. Otolaryng. 56:504-511, 1952.

Announcing a scientifically significant development in cigarette smoking...

KENT

with the exclusive "MICRONITE" FILTER

DOCTORS have long been aware of the need for a really effective filter-tipped cigarette. P. Lorillard Company has been conscious of this problem, and after years of study, experiment and research believes it has developed a cigarette that meets the need.

It is the new KENT cigarette with the "Micronite"* Filter. Recent tests have shown that the Micronite Filter *approaches 7 times the efficiency of other filters in the removal of tars and nicotine* and is virtually twice as effective as the next most efficient cigarette.

All members of the medical profession will be interested in the facts about this new cigarette. To avoid possible confusion or misunderstanding by the general public, the details of the KENT studies given on these pages are for physicians only, and will not appear in KENT advertising or promotion to the general public.

Micronite as a cigarette filter...

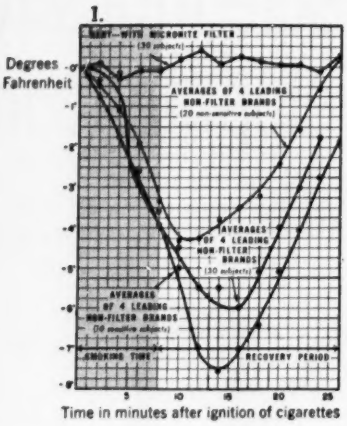
The new filter material—called Micronite—stems directly from the improved protective filters developed to meet critical air-purification problems in atomic energy plants.

When investigations showed that this filter medium was capable of removing all of the minute particles from a stream of cigarette smoke, the filter was modified for use in KENT cigarettes. *This was done in such a way as to permit the passage of pleasant aromatic smoke constituents, but with a removal of the more objectional fractions of tobacco smoke to an extent never before accomplished.*

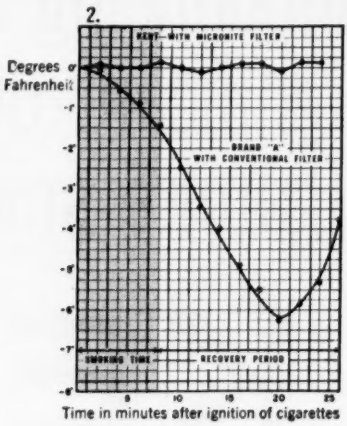
Efficacy of the Micronite Filter

The normal human subjects used in testing the Micronite Filter were divided into two categories—*susceptible and non-susceptible*—on the basis of their sub-

*PATENT APPLIED FOR



1. Comparison of KENT with leading non-filter brands. Effects on Peripheral Vascular System. Drop in surface skin temperature at the last phalanx induced by smoking one cigarette.



2. Comparison of KENT with Brand "A" conventional filter tip. Effects on Peripheral Vascular System. Drop in surface skin temperature at last phalanx induced by smoking one cigarette. Average for 15 susceptible subjects.

jective reactions to cigarette smoking. Approximately two-thirds of the subjects *in this investigation* were *non-susceptible* while the remaining third were definitely *susceptible*. Other investigations have reported a somewhat similar ratio. (a)

To study the effects of this filter on physiological reactions to cigarette smoke, in both *susceptible and non-susceptible persons*, two different tests were employed, both being measurements of peripheral blood flow.

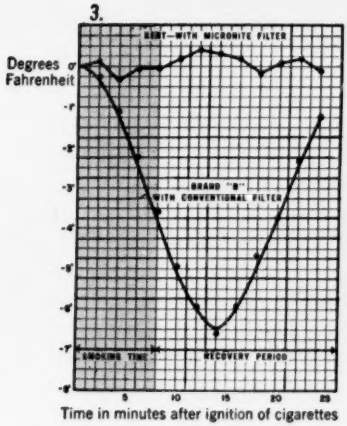
The first test involves the drop in skin temperature occurring at the finger tip, induced by smoking and measured according to *well-established procedures*. (b, c)

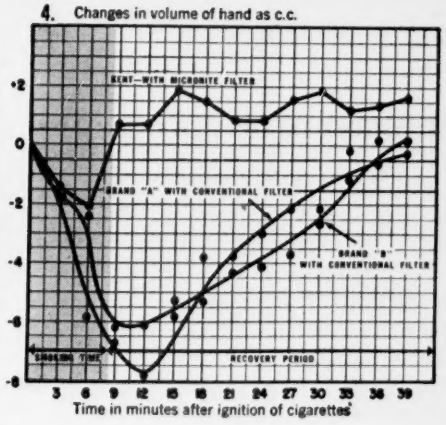
The second test is a measurement of vasoconstriction in the hand, as recorded plethysmographically. (d)

The results of these measurements—determined for Lorillard by an independent research organization—are shown on the four charts reproduced here. Concurrently, other outside independent laboratories are carrying on further research on the chemical and physiological effects of cigarette smoking *with new and original testing methods*.

From these charts, the following general conclusions may be drawn:

When cigarette smoke is drawn through a Micronite Filter, it is no longer capable of producing characteristic changes in pe-





3. Comparison of KENT with Brand "B" conventional filter tip. Effects on Peripheral Vascular System. Drop in surface skin temperature at the last phalanx induced by smoking one cigarette. Average for 15 susceptible subjects.

4. Comparison of KENT with Brand "A" and "B" conventional filter tip. Peripheral vasoconstriction induced by smoking one cigarette. Peripheral blood flow as measured by continuous plethysmography on the hand. Average for 4 susceptible and 8 non-susceptible subjects.

ripheral blood flow in either susceptible or non-susceptible persons.

The Micronite Filter is vastly superior to any other available filter now in use for removing tars and nicotine in cigarette smoke.

Here are additional observations from work now in progress:

1. When smoke which has passed through a Micronite Filter contacts the conjunctival sac of the rabbit, far less irritation occurs than when the sac is exposed to the smoke from regular cigarettes or the smoke from popular filter-tipped brands.

2. Current studies also indicate that Micronite-filtered smoke is less irritating to mucous membranes than unfiltered smoke.

When the scientific evidence of the effectiveness of the Micronite Filter is compared *with* the effectiveness of other filters, *it shows that*—

The problem of smoker susceptibility to tobacco irritants may be largely overcome by KENTs. And for those people whose smoking should be restricted for therapeutic reasons, KENT should be considered as the cigarette of choice.

P. Lorillard Company will gladly send you a booklet, prepared especially for the medical profession, which describes more fully the investigational work on the chemical and physiological advantages of the new Micronite-filtered KENT cigarette.

References Cited

a. *A Manual of Pharmacology*, 7th edition, Philadelphia, W. B. Saunders Co., 1949, pp. 341-352.

b. *J.A.M.A.*, Vol. 103, 1934, p. 318.

c. *J.A.M.A.*, Vol. 135, 1947, p. 417.

d. *J.A.M.A.*, Vol. 104, 1935, p. 1963.

Premature heart contractions should be controlled by quinidine or procaine amide before operation.

Supraventricular Tachycardia and Surgery

WAYNE R. ROGERS, M.D., FELIX WRÓBLEWSKI, M.D., AND JOHN S. LA DUE, M.D.
Memorial Center for Cancer and Allied Diseases, New York City

PERSISTENT postoperative supraventricular tachycardia, despite adequate therapy, is a bad prognostic sign. Cardiac failure caused by, or associated with, arrhythmia responds poorly to treatment.

Although no prediction can be made as to whether cardiac arrhythmias will develop as a complication of surgery, heart disease is usually evident preoperatively, state Wayne R. Rogers, M.D., Felix Wróblewski, M.D., and John S. LaDue, M.D. The occurrence of auricular or ventricular premature contractions preoperatively justifies the control of these irregularities by means of quinidine or procaine amide.

The complication is most frequently seen with chest surgery. Intraoperative systolic hypotension of 100 mm. of mercury or less and postoperative cardiopulmonary complications appear to be causally related to the onset of the arrhythmias. Anemia, fever, and parenteral administration of fluids or blood apparently have no causal relationship.

One-fifth of abnormal rhythms start during the operation. Trauma to the heart or to related autonomically innervated structures, cardiac arrest, and pulmonary edema are often precipitating causes. The type of anesthesia used seems to be inconsequential.

Abnormalities of cardiac rhythm which develop during or after surgery respond slowly to therapy, probably because of the serious organic disease responsible for development of the irregularity. The arrhythmia is usually auricular fibrillation but auricular flutter, nodal tachycardia, auricular tachycardia, and flutter-fibrillation also occur.

The best treatment is prompt digitalization, preferably intravenously, with 1.6 mg. of lanatosid C within a period of five minutes to patients who are not receiving maintenance doses of digitalis. The initial dose is followed by 0.2 mg. of digitoxin daily and change is made thereafter according to accepted standards. If the arrhythmia persists for forty-eight hours, quinidine is given in dosages of 0.4 to 0.6 gm. every three hours until the irregularity reverts or toxicity develops.

Although procaine and procaine amide are considered relatively ineffective in supraventricular tachycardia, these agents are desirable

Supraventricular tachycardia complicating surgical procedures. Circulation 7:192-199, 1953.

when digitalis or quinidine, or both, have proved ineffective. If the irregularity persists after forty-eight hours of quinidine and digitalis treatment, an infusion of 1,000 cc. of procaine, 0.1% in 5% glucose, should be started. Instead of procaine, procaine amide may be given intravenously at the rate of 200 mg. per minute up to a total of 1 gm. or until the arrhythmia ceases.

With these methods, most supraventricular arrhythmias revert to sinus rhythm. Both digitalis and quinidine are continued until the patient is fully ambulatory, or longer if other indications exist.

The patient who is taking maintenance digitalis when paroxysmal tachycardia develops is treated at once with quinidine and other medications as described.

Prompt attention to possible precipitating causes such as fluid and electrolyte imbalance and pulmonary and renal complications is needed besides specific therapy.

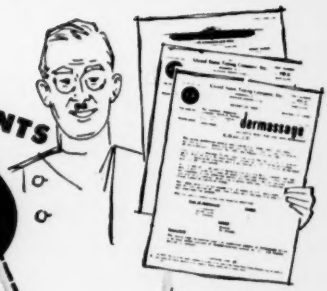
Response to treatment is not immediate, the average duration of arrhythmia being thirty hours. No permanent damage results from arrhythmia of this duration.

If treatment is not prompt and arrhythmia not stopped, the mortality rate is high. Death may result from heart failure, myocardial infarction, or cardiac arrest. The heart failure which develops is extremely refractory.

NO BETTER THAN ITS INGREDIENTS

A product is

...Especially
A PRODUCT FOR PATIENT PROTECTION



LABORATORY REPORTS support experience—offer explicit data on the positive protection afforded by Dermassage.

EVER SINCE physicians and hospital executives discovered eighteen years ago that Dermassage was doing a consistently good job of helping to prevent bed sores and keep patients comfortable, lotion type body rubs of similar appearance have been offered in increasing numbers.

But how many professional people would choose *any product for patient use* on the basis of appearance?

DERMASSAGE *protects the patient's skin effectively and aids in massage because it contains the ingredients to do the job.*

It contains, for instance: LANOLIN and OLIVE OIL—*enough* to soothe and soften dry, sheet-burned skin; MENTHOL—*enough* of the genuine Chinese crystals to ease ordinary itching and irritation and leave a cooling residue; germicidal HEXACHLOROPHENE—*enough* to minimize the risk of initial infection, give added protection where skin breaks occur despite precautions. With such a formula and a widespread reputation for silencing complaints of bed-tired backs, sore knees and elbows, Dermassage continues to justify the confidence of its many friends in the medical profession.

Where the patient's comfort in bed (1) contributes in some measure to recovery, or (2) conserves nursing time by reducing minor complaints, you *cannot afford* a body rub of less than maximum effectiveness. You can depend upon Dermassage for effective skin protection *because it contains the ingredients to do the job.*

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Strips stain and debris from instruments and leaves them film-free after a 10-to-20 minute immersion in Edisonite "chemical fingers" solution. Harmless to hands, as to metal, glass and rubber.
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Excision of the uterus vaginally contravenes many complications often seen after abdominal removal.

Use of Vaginal Hysterectomy

VIRGIL S. COUNSELLER, M.D.
Mayo Clinic, Rochester, Minn.

SAFETY is one of the greatest assets of vaginal removal of the uterus. The procedure can often be used instead of abdominal hysterectomy or vaginal plastic operations.

Since vaginal hysterectomy is almost entirely extraperitoneal, peritoneal contamination is slight. The anesthesia need not be as profound as for abdominal hysterectomy, and complications such as pneumonia and atelectasis are rare. Little blood is lost and blood pressure is seldom lowered, so that the patient who is a poor risk for abdominal surgery can withstand a similar operation by the vaginal route.

One of the most common indications for vaginal hysterectomy is uterine prolapse in women over 40 years of age. Vaginal plastic surgery may also be done at the same time, and the adnexa can be easily inspected and removed if necessary.

Menorrhagia and metrorrhagia before the menopause caused by fibroids smaller than a fetal head are better treated by vaginal uterine excision than by a menopausal dose of radium. Extensive bleeding in young women caused by ovarian dysfunction, and uncontrollable by medical therapy, can be treated satisfactorily by vaginal hysterectomy, the ovaries being left if normal.

Recurring uterine polyps, chronic endometritis, and pyometra may be precancerous lesions and are perhaps best cared for by removing the uterus vaginally. Carcinoma of the fundus usually occurs after the menopause in women who are poor operative risks. As radical an operation can be done vaginally as by an abdominal approach, except for the lymph node dissection, which is rarely indicated. Repair of the anterior and posterior walls is avoided because of the possibility of an implant in the suture line.

If future childbearing is not a factor, vaginal hysterectomy may be done for carcinoma in situ. In a young patient, the adnexa can be left, if normal. When cervical invasion is found after the procedure, dissection of the iliac and obturator nodes by an abdominal operation should be done.

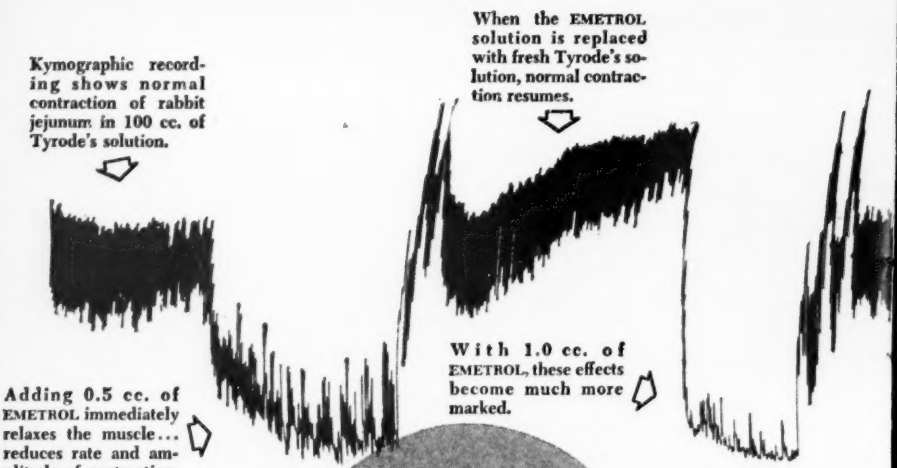
For uncontrolled dysmenorrhea with extreme disability, when the expectation of bearing children has been abandoned, vaginal hysterectomy can be easily performed.

The procedure should not be used with extensive adnexal disease or any disease attended by considerable fixation. Previous pelvic abdominal operations, especially uter-

(Continued on page 175)

Vaginal hysterectomy. Obst. & Gynec. 1:84-93, 1953.

• Modern centrifuge



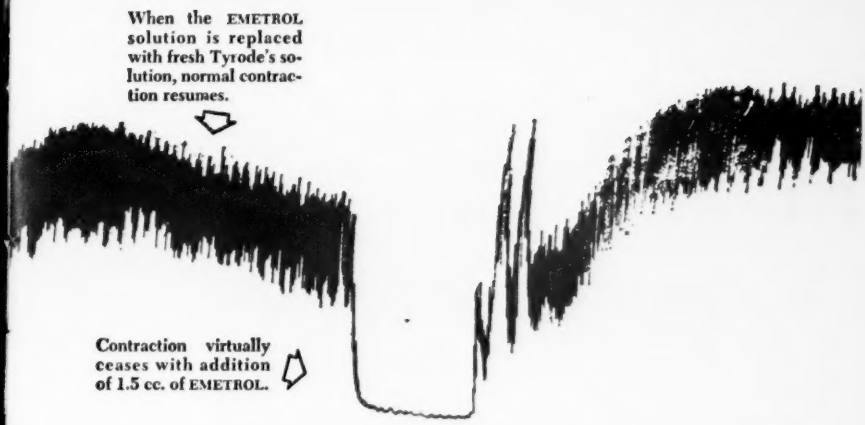
this is why EMETROL® controls

(PHOSPHORATED CARBOHYDRATE SOLUTION)

EMETROL Phosphorated Carbohydrate Solution permits effective physiologic control of functional nausea and vomiting—without recourse to antihistaminics, sedatives, or hypnotic drugs.

Pleasantly mint flavored, EMETROL provides balanced amounts of levulose and dextrose in coacting association with orthophosphoric acid, stabilized at an optimal, physio-

Kinney® SAMPLE AND LITERATURE



epidemic vomiting physiologically

logically adjusted pH level.

Thus, EMETROL can be given *safely* —by teaspoonfuls for children, tablespoonfuls for adults—at *repeated* intervals until vomiting ceases.

IMPORTANT: EMETROL is always given *undiluted.* No fluids of any kind should be taken *for at least 15 minutes after taking* EMETROL.

INDICATIONS: Nausea and vomiting resulting from functional disturbances, acute infectious gastroenteritis or intestinal "flu," pregnancy, motion sickness, and administration of drugs or anesthesia.

SUPPLIED: Bottles of 3 fl. oz. and 16 fl. oz., at all pharmacies.

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TO PHYSICIANS ON REQUEST

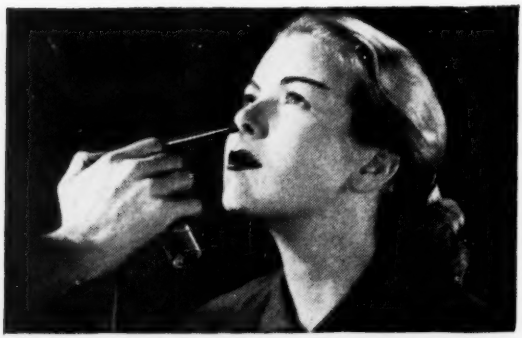
For refractory nasal infections,

as OZENA: ***FURACIN***

A nonirritating bactericide:

FURACIN NASAL

plain & with ephedrine



Marked or complete relief of symptoms of refractory cases of ozena, resulted from the use of Furacin Nasal plain by spray every two hours.

Reference: Thornell, W. C.: *Ozena. Streptomycin and Nitrofurazone Therapy,* Arch. Otolaryng. 52:96, 1950.

Literature on request

Some advantages of Furacin:

- no slowing of ciliary action
- no delay of healing
- no interference with phagocytosis
- no inhibition of nasal lysozyme

Formulae: *Furacin Nasal plain* contains Furacin 0.02% ® brand of nitrofurazone N.N.R. in isotonic, aqueous solution. *Furacin Nasal with ephedrine* contains in addition, ephedrine •HCl 1%. 1 fl. oz. bottles.

EATON Laboratories Inc.
NORWICH, NEW YORK

OTHER DOSAGE FORMS OF FURACIN INCLUDE:

FURACIN SOLUBLE POWDER • FURACIN VAGINAL SUPPOSITORIES

ine suspension, may complicate a vaginal type of hysterectomy.

At surgery, Virgil S. Counseller, M.D., pulls the cervix down and injects Pituitrin to aid hemostasis. The vaginal wall is then incised around the cervix and pushed upward. The pubocervical and rectovaginal fasciae are incised, exposing the peritoneum of both cul-de-sacs.

The peritoneum is opened posteriorly and the adnexal areas explored with the finger. Uterosacral and cardinal ligaments are divided between clamps and ligated on each side.

With the bladder retracted, the uterine fundus is withdrawn from the pelvis, anteriorly or posteriorly, and the round and ovarian ligaments are divided and ligated together, allowing the uterus to be removed.

The peritoneum is then closed with a running suture, being tied to bring the stumps of the round and ovarian ligaments outside the peritoneal cavity. The uterosacral and cardinal ligaments are reattached separately to the angles of the vagina. Shortening of the ligaments is necessary if relaxation is considerable. Interrupted sutures are used to close the pubocervical and rectovaginal fasciae together with the vaginal wall.

Plastic repair of a rectocele or cystocele may be done at the end of the procedure.

Pediatric pathology is not a miniature of the adult picture but is peculiar to infant diseases.

Pulmonary Insufficiency in the Newborn

HELEN MORTON, M.D., G. R. HENNIGAR, M.D., AND LEE E. SUTTON, JR., M.D.
Medical College of Virginia, Richmond

THE majority of neonatal deaths are caused by pulmonic insufficiency. The pattern of disease in the tissues of the infant differs from that of the adult. Until each of the causes is understood, effective specific therapy will not be available, believe Helen Morton, M.D., G. R. Hennigar, M.D., and Lee E. Sutton, Jr., M.D.

In utero the lumina of the bronchial tree are bathed in amniotic fluid. Few alveoli are expanded by fluid. However, when the placenta fails to provide sufficient oxygen, gasping respiratory movements occur which suck the fluid deep into the immature alveoli.

Primary atelectasis, the chief cause of death in the immature premature, is most common in the 2- to 3-lb. infant who breathes poorly at birth, fails to respond to treatment, and dies in a few hours. Grossly, the lungs are beefy, red, and airless; these lungs are identical with those of a stillborn. Microscopically, the majority of the alveoli have never expanded. Expansion with later collapse occurs in the secondary type.

Primary atelectasis is rare in the 4- to 7-lb. infant unless concomitant structural or functional abnormalities exist.

Secondary or *resorption atelectasis* is a common complication of subarachnoid hemorrhage, tentorial tears, and bacterial meningitis. When intracranial hemorrhage is the cause, labor and delivery have been difficult. The intracranial lesion presumably produces respiratory paralysis; death ensues in a few hours. Grossly, depressed purple areas are seen sharply demarcated from normal areas. Histologically, alveolar hemorrhage and areas of entrapped air are seen.

Secondary atelectasis occurs in any weight range. A premature or term infant, who has done well for at least a week, may suddenly become listless, anorexic, and have diarrhea or convulsions.

Pulmonary hyaline membranes in prematures are composed chiefly of protein with little or no cells or vernix. Usually symptoms appear after only a few hours. Membranes lie tenaciously against the alveolar walls and have an eosinophilic, homogeneous, glassy appearance.

Vernix pneumonia with membrane formation occurs only at or near term following complications of parturition. Severe respiratory

Pulmonary insufficiency in the newborn. South. M. J. 46:1-7, 1953.

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distress may be apparent at birth or may not appear for several hours. This condition may be distinguished from true hyaline membrane formation by the presence of vernix and squamous cells and the appearance of bacterial pneumonia in 90% of cases. Broad-spectrum antibiotics, given immediately, may be lifesaving.

The near term or term infant with *alveolar dysplasia* is cyanotic at birth, lives one or two weeks, then dies suddenly. Persistent pulmonary mesenchyma and greatly thickened alveolar septa are found.

Mononuclear pneumonia, or interstitial pneumonitis, usually occurs at about 1 year of age but is occasionally seen toward the end of the neonatal period. In a well baby, coryza of one to seven days duration is often the only symptom. Roentgenograms show increased bronchial and pulmonary markings. Sudden death is common. Scattered red-purple areas of consolidation, edematous appearance of the lungs, and subpleural petechial hemorrhage are found post mortem. The scattered areas of involvement show edema, congestion, and hemorrhage into alveoli.

Histamine and Cerebral Ischemia

A. R. FURMANSKI, M.D.

CHANCES of improvement with ischemia of the brain are at least doubled by histamine therapy, concludes A. R. Furmanski, M.D., of Studio City, Calif., after treating 50 patients with varying degrees of neurologic dysfunction. Response is more likely to be good if the initial neurologic dysfunction is of only slight degree and short duration and if the patient is under 60, not comatose or stuporous, and without cardiac insufficiency.

Intravenous infusions are given of 5.5 mg. of the phosphate of histamine in 1,000 cc. of 5% dextrose in saline. The injection is begun at the rate of 20 drops per minute and is then increased in steps by 5 or 10 drops after intervals of two or three minutes if no facial flush develops. Seldom need 80 drops per minute be exceeded. The proper speed of infusion for each patient is fairly constant and, once determined, can be repeated later. The infusion lasts four to six hours and is given twice daily until improvement has been maintained for two or three days. If no benefit is apparent after a two-week trial, histamine therapy is abandoned.

Dextrose is omitted for diabetic patients and the salt for patients taking salt-restricted diets. The volume of vehicle can be lowered, with reductions of injection rate, when fluid intake is limited.

Histamine therapy in acute ischemia of the brain. Arch. Neurol. & Psychiat. 69:104-117, 1953.

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*COPPER	0.7 mg.	FOLIC ACID	0.05 mg.
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*IODINE	0.15 mg.	PANTOTHENIC ACID	3.0 mg.
*IRON	12 mg.	PYRIDOXINE	0.6 mg.
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*Nutrients for which daily dietary allowances are recommended by the National Research Council.

Confident reassurance of the victim of subarachnoid bleeding is an essential part of rehabilitation.

Sequelae of Subarachnoid Hemorrhage

JOHN N. WALTON, M.D.
Royal Victoria Infirmary, Newcastle-upon-Tyne, England

THE individual who has survived a subarachnoid hemorrhage is often invalided unnecessarily by the physician's mistaken belief that exertion will increase the possibility of fatal recurrence. Warned to be quiet, the patient may become fearful of any activity; an anxiety neurosis develops and work is given up.

Studying 312 patients with spontaneous hemorrhage admitted to a hospital during a nine-year period, John N. Walton, M.D., found that 140, or 45%, died during the first illness or from a recurrence within the first eight weeks. Of the 172 who lived longer, 170 were traced.

Among the 170 living beyond eight weeks, slightly more than one-fifth—35 persons—died later of hemorrhage. Half of these fatal recurrences happened during the first six months after discharge from the hospital following the original illness. Significantly more females than males died of second hemorrhages.

Exertion or a temporary rise in blood pressure is often considered the cause of recurrence, but exertion could be clearly implicated in but 4 of the 22 recurrences in which adequate information was obtainable.

Of the 120 survivors, nearly two-thirds are fully employed today, 20% are in a lighter occupation, 10% have retired but are active, and only 4.2% are unable to work. Of this same group, 30% are considered completely well, 33.3% have slight sequelae, 32.5% have moderate or severe sequelae, and 4.2% are completely disabled.

Residual sequelae include paralytic manifestations, convulsions, headache, and mental symptoms and are similar in many ways to those of head injury. As in head injury, patients with unsatisfactory previous personalities are more likely than others to have the post-traumatic syndrome. In every case, adequate reassurance and careful management are important.

Each case must be considered individually, but when recovery has been good, overcaution is unnecessary. Usually, the possibility of recurrence should never be mentioned to the patient.

Surgery seems unjustified after eight weeks, because the possibility of another bleeding has become less than the risk of craniotomy. Ligation of the carotid artery in the neck may be considered when aneurysm of the carotid artery has been demonstrated, but this procedure is not without risk.

The late prognosis of subarachnoid hemorrhage Brit. M. J. 4788:802-808, 1952.

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Medical Forum

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Anesthesia for Adult Tonsillectomy*

QUESTION: Is use of Sodium Pentothal, curare, pontocaine, and novocain without endotracheal intubation advisable as anesthesia for adult tonsillectomies?

Comment invited from
Clarence H. Steele, M.D.
Milton S. Lloyd, M.D.
John J. Bonica, M.D.
Charles L. Burstein, M.D.

► TO THE EDITORS: I enjoyed reading Dr. Fordyce Johnson's article on anesthesia for adult tonsillectomy. Use of Sodium Pentothal and curare for tonsillectomy admittedly has the advantage of high patient acceptance but confronts the surgeon and anesthesiologist with a number of hazards which necessitate an exacting technic. I shall call attention to a few of these.

To minimize the tendency for laryngospasm, a constant threat during Sodium Pentothal anesthesia in any operative procedure on the airway, effective topical anesthesia should be secured in the pharynx, the hypopharynx, and the larynx.

Even though one uses the Rose position with the Davis-Crowe gag in place, aspiration of secretions is an ever present danger. Constant observation of the hypopharynx and larynx is necessary, with frequent suction.

As Sodium Pentothal has a depressant effect on respiratory excursion, compared to most inhalant anesthetic agents employed in tonsillectomy, it is advantageous to insufflate oxygen through the anesthesia tube attached to the tongue blade of the Davis-Crowe gag. Anoxia or hypoxia is much less likely to occur when this technic is followed.

Of great importance is meticulous attention to hemostasis, aspiration of the tracheobronchial tree at the close of operation, and accurate control of anesthesia at the end of surgery to avoid a prolonged period of unconsciousness after the patient leaves the operating room. Returning the patient to a recovery ward, with trained personnel and resuscitative equipment instantly available, is a technic at present nonexistent in many hospitals, but such a procedure is almost mandatory when Sodium Pentothal is the anesthesia used for tonsillectomy.

CLARENCE H. STEELE, M.D.
Kansas City, Kan.

*MODERN MEDICINE, Dec. 15, 1952, p. 98.

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► TO THE EDITORS: Although I am not an otolaryngologist, I feel closer to the subject, because of my experience in peroral endoscopy, than the clergyman who invented the laryngeal mirror.

General anesthesia, unless very deep, does not obtund the cough reflex and, consequently, does not prevent laryngospasm if the larynx is invaded. Any procedure, therefore, which avoids the laryngeal vestibule should be safely feasible under Sodium Pentothal anesthesia, as long as the pharynx is dry and inspiration of foreign material is prevented. This would include tonsillectomy, performed with proper precautions.

On the other hand, use of this drug as anesthesia for esophagoscopy without preliminary intubation is dangerous, because it is difficult to perform an esophagoscopy without stimulating cough.

My opinion would be that Sodium Pentothal is a satisfactory anesthesia for tonsillectomy when employed by the meticulous surgeon. Otherwise, intubation should be done in advance in order to avoid difficulty and even death on the table.

MILTON S. LLOYD, M.D.
New York City

► TO THE EDITORS: I feel that any anesthetic technic for tonsillectomy which omits endotracheal intubation is inadvisable for general use because the patient is not afforded the optimum degree of safety. Notwithstanding Dr. Johnson's impressive record, for which he and his staff should be commended, the technic of using topical pontocaine, followed by intravenous Pentothal-syncurine and procaine infiltration without intubation, does not preclude the dangers inherent in the use of general anesthesia for surgical procedures of the mouth and throat.

The primary responsibility of the anesthesiologist in these cases is to afford the patient adequate oxygenization by assuring a patent airway. This cannot always be done without a tube because the relaxed tongue, pharyngeal muscles, epiglottis, instruments, and the surgeon's hands frequently encroach upon the airway, regardless of the type of mouth gag that is employed.

Before we adopted endotracheal intubation as a routine procedure, aspiration of blood into the tracheobronchial tree occurred more frequently than in 1% of cases, in spite of constant suction and head down position. This is a particular danger when bleeding is very active.

The technic described does not obviate the dangers of Pentothal Sodium because, unless one waits five to eight minutes after the throat is sprayed, the possibility of laryngeal spasm still exists, since this amount of time is necessary for complete surface anesthesia with pontocaine.

Even if topical anesthesia is complete, this technic does not eliminate the dangers of aspiration. Although this drug does not stimulate the vomiting center, regurgitation and consequent aspiration of

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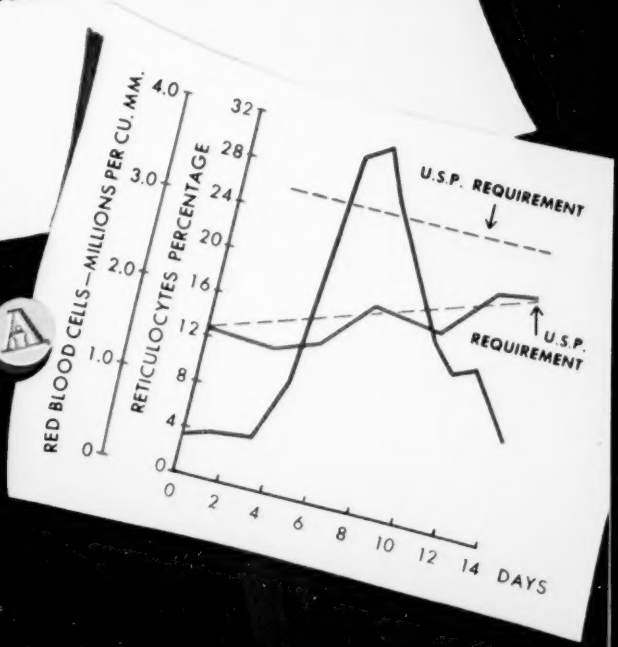

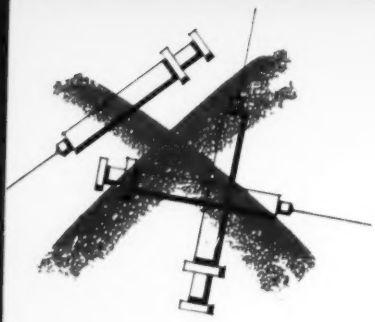

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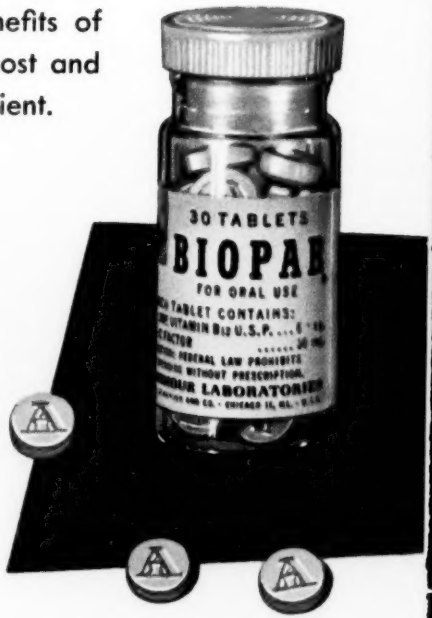

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PHYSIOLOGIC THERAPEUTICS THROUGH BIORESEARCH

stomach contents can and do occur during Pentothal anesthesia as with any general anesthetic.

Clinical investigations by Weiss (*Anesthesiology* 11:102-109, 1950) and by Culver, Makel, and Beecher (*Ann. Surg.* 133:289-292, 1951) by the dye method have revealed that a significant number of patients regurgitate during general anesthesia, and that, of these, a high percentage aspirate the gastric contents into the lungs. Culver and associates found that this complication is enhanced when the Trendelenburg and prone positions are employed.

Not infrequently, this regurgitation occurs without any apparent signs. With the technic described, silent regurgitation is very likely because of the relaxant effects of Pentothal-syncurine. Moreover, obtundation of laryngeal reflex with the surface anesthesia facilitates silent aspiration.

The 10° Trendelenburg position employed is not sufficient to prevent sudden aspiration of foreign material into the tracheobronchial tree. Since topical anesthesia with pontocaine usually outlasts the tonsillectomy operation, it would seem that the real danger of aspiration arises after the patient leaves the operating pavilion, because the "watchdog of the lungs," the laryngeal reflex, is absent.

I would like to reemphasize that an endotracheal tube should be introduced in all patients, regardless of age or duration of operation, who are to undergo surgery of the mouth and throat under general anesthesia.

The possible dangers of hypoxia, anoxia, and pulmonary complication without intubation are far greater than those inherent in intubation when done by a competent individual.

JOHN J. BONICA, M.D.
Tacoma

► TO THE EDITORS: In my opinion, the technic advocated by Dr. Fordyce Johnson for anesthesia in adult tonsillectomy is dangerous. A report of 189 cases is too small to recommend adoption of such a procedure.

In the first place, too many drugs are utilized, any or all of which may be toxic, particularly if respiratory obstruction with oxygen lack should develop.

Secondly, this technic, even in the hands of expert anesthesiologists, would not furnish the optimum conditions for tonsillectomy. A somnifacient dose of Sodium Pentothal would not permit relaxation of the jaw muscles.

Topical anesthesia with pontocaine does not guarantee against the production of laryngeal spasm when the glottis is stimulated during Sodium Pentothal administration. On the other hand, during the immediate posttonsillectomy period, the laryngeal reflex may be so obtunded that aspiration of blood and vomitus may occur. The vital requirements of a patent nonobstructed airway and protection against aspiration of foreign matter are not satisfied.

CHARLES L. BURSTEIN, M.D.
New York City

Diagnostix

Here are diagnostic challenges presented as they confront the consultant from the first clue to the pathologic report. Diagnosis from the Clue requires unusual acumen and luck; from Part II, perspicacity; from Part III, discernment.

Case MM-239

THE CLUE

ATTENDING M.D: The next patient, a 31-year-old housewife, was admitted to the hospital ten days ago because of severe dyspnea, cyanosis, hemoptysis, and syncope.

VISITING M.D: Certainly an ominous collection of symptoms. Why didn't I see her last week?

ATTENDING M.D: By the morning after admission she was feeling quite well—no orthopnea and the hemoptysis amounted to only about 2 oz. of bright blood and did not recur. Her sensorium has been clear since regaining consciousness. The syncopal attack lasted only a few minutes.

VISITING M.D: How about the dyspnea and cyanosis?

ATTENDING M.D: As I said, she is perfectly comfortable while lying flat in bed but slight exertion does cause dyspnea. The cyanosis is still present but amounts to only blueness of the fingernails which, by the way, are slightly clubbed.

VISITING M.D: Enlarge on the history, please.

ATTENDING M.D: The first symptom noted appeared about three years ago—dyspnea from moderate exertion. She also had a nonproductive cough. A chest film made at the time was reported to be negative. The dyspnea has become progressively more noticeable and, about one year ago, her husband commented on the blueness of her fingers. This sign has not been constantly present but her nails do become cyanotic frequently. No other symptoms have been noted.

VISITING M.D: And the acute episode?

ATTENDING M.D: For about a week before she came to the hospital, her breathing was quite labored.

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Then the evening of admission she suddenly coughed up bright blood and fainted. The story certainly suggested heart disease to me, but I am confused by the lack of orthopnea.

PART II

VISITING M.D: That is strange and certainly suggests that the dyspnea is not the result of pulmonary congestion. Emphysematous patients sometimes notice improvement of breathing when lying flat.

ATTENDING M.D: That seems unlikely here. Her vital capacity is 4.2 liters and expiration is rapid. The patient's room is down the hall.

VISITING M.D: *(After completing his examination)* I'm almost sure this is an unusual disease we are dealing with. Her respiratory motions are normal and by auscultation the lungs are clear, yet the slight effort of sitting up in bed made her short of breath. Percussion does not show the heart to be enlarged and I could hear no murmurs despite careful listening. The second pulmonic sound is loud, the rhythm regular, and blood pressure normal. The remainder of the physical examination is negative. There are no neurologic abnormalities; eyegrounds are normal, and reflexes intact. Nothing suggests thrombophlebitis.

ATTENDING M.D: Could you feel the liver?

VISITING M.D: Yes, on deep inspiration the liver edge was palpable a few centimeters below the costal margin, but the patient has no edema or ascites. Do

(Continued on page 192)

Doctor to Doctor

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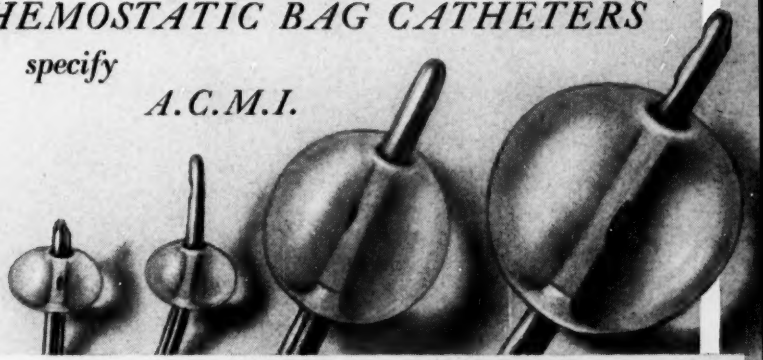

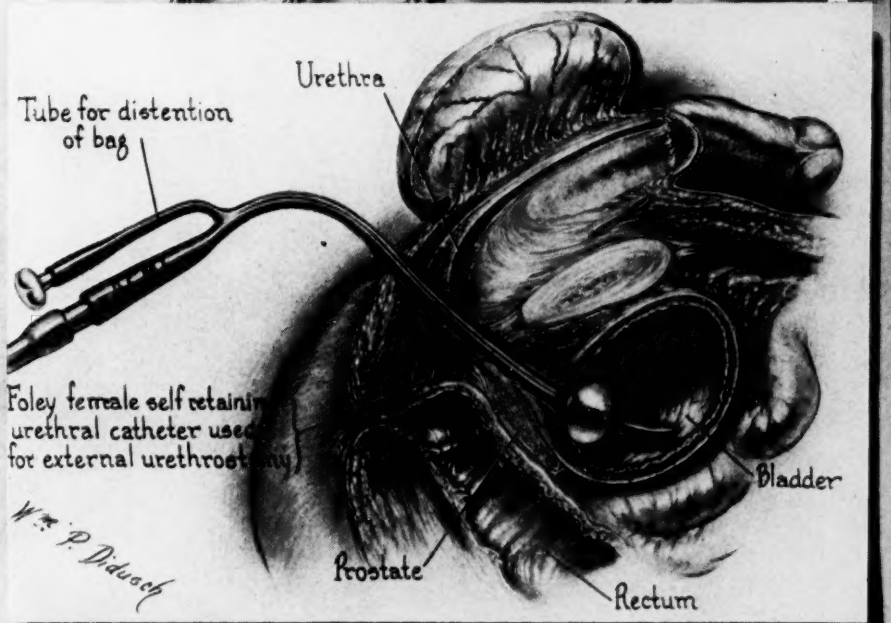

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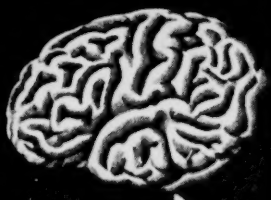

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*Harmann, I. F., and Smith, R. T.: JL.- Lancet 71:271 (July), 1951.

you have the report of the fluoroscopic examination?

PART III

ATTENDING M.D: The heart was not enlarged in the posteroanterior view and the lung fields were clear. However, the pulmonary artery was prominent and, in the right anterior oblique view, the right ventricle appeared somewhat enlarged.

VISITING M.D: How about pulmonary artery pulsation?

ATTENDING M.D: The roentgenologist thought it normal or only slightly increased.

VISITING M.D: We have no evidence of pulmonary disease or an intrinsic cardiac disorder such as mitral stenosis, yet the fluoroscopic report and the loud pulmonic second sound would suggest high pressure in the pulmonary circuit. We shall probably have to recommend cardiac catheterization.

ATTENDING M.D: The remaining laboratory reports show a polycythemia with hemoglobin of 18 gm. and a red cell count of 6,000,000. The electrocardiogram reveals right axis deviation with an early strain pattern. What diagnosis are you considering?

VISITING M.D: I believe the situation demands a diagnosis by exclusion. The disease I have in mind is uncommon and not much is known about it. The differential diagnosis must include all causes of pulmonary hypertension. Cardiac catheterization should be very helpful.

ATTENDING M.D: *(One week later)* The patient we saw last week continues to feel well and withstood cardiac catheterization well. Here are the results: cardiac index 2.9, arterial oxygen saturation 86%, elevated systolic pressure in the right ventricle of 70/10 mm. of mercury, and elevated systolic and diastolic pressure in the pulmonary artery at 70/32 mm. of mercury. The contour of the pressure tracings was normal and there was no evidence of left to right shunt in the oxygen content of blood from the right atrium and ventricle and pulmonary artery.

PART IV

VISITING M.D: That pretty much leaves us with the rather unsatisfactory diagnosis of primary pulmonary hypertension. There is no primary cardiac disease or emphysema and nothing appears to suggest a thromboembolic affair.

ATTENDING M.D: What treatment do you recommend?

VISITING M.D: As with essential hypertension of the systemic circuit, there is nothing specific to offer at this point. Probably the right heart will eventually fail and then supportive treatment will be needed. The prognosis is poor in most cases, although the fact that most diagnoses of this illness are made post mortem may give us a falsely pessimistic outlook. To clinch the diagnosis, a lung biopsy would be necessary. At present, I feel that this is not indicated.

SHORT REPORTS FROM ABROAD

FRANCE

Bone Graft Conservation. In a big surgical hospital the bone bank is an established unit. However, quick availability of an adequate quantity of good graft material is of prime importance. The preservation and transportation of frozen homografts remain a cumbersome and costly procedure, as is the conservation of bone in different antiseptic solutions. The ideal arrangement would be for the surgeon to be able to choose the desired size of bone as easily as picking silk or catgut.

Dr. R. Dubau and associates of Percy Hospital and the Army Reanimation and Transfusion Center, France, prepare bone grafts suitable for convenient storage, transportation, and immediate utilization by freezing, vacuum desiccation, and sealing in airless tubes.

The bone is placed in a sterile tube, immediately frozen to −35° C. or lower, then desiccated under vacuum, 0.15 to 0.07 mm. of mercury, for thirty-six hours to fourteen days, depending on the size and thickness of the bone. After desiccation, the bone is placed in a tube filled with nitrogen and sealed.

Conservation is excellent if the humidity is below 1%. To insure better sterility, the bone may be placed in an antibiotic solution during the desiccation.

For use the tube is opened and the bone conserve put in place. Rehydration is necessary when the size has to be adjusted or holes drilled, the graft being brittle. However, allowing the graft to be rehydrated in situ by the recipient's body fluids increases the specificity.

2

Trephine and Ventricular Puncture. Trephination is indicated for tuberculous meningitis in children whenever intracranial pressure is high or subdural injection of antibiotics is necessary. With papillary edema, separation of the cranial sutures, and unconsciousness, trephination is urgent.

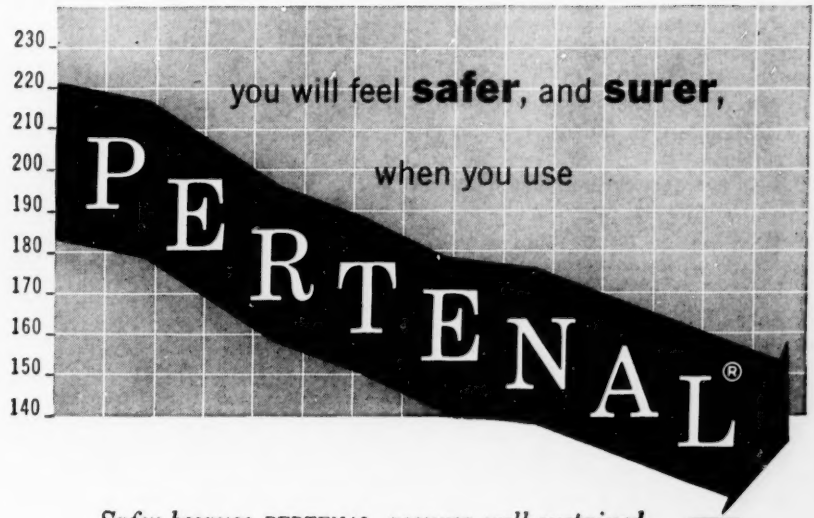
Ventricular taps may be performed daily, if necessary, but should not be done more than twice a day, according to Dr. R. Debré and associates of Paris. The younger the child and the smaller the rise in the spinal fluid protein content, the better the survival rate.

In 78 of 158 children treated by trephine and ventricular puncture, improvement was evident after a week. No improvement after that period is an unfavorable prognostic sign.

3

Determination of Portal Circulation Time. The slowing of the portal circulation produced by portal hypertension is not usually apparent clinically until the obstruction reaches a certain level. Dr. Jean

in **hypertension**



Safer because PERTENAL *assures well-sustained lowering of pressure, and prompt control of distressing symptoms, without fear of serious toxic reaction.*

Surer because PERTENAL *is a comprehensive approach to the problem.*

PERTENAL combines:

1. The DUAL HYPOTENSIVE ACTION of veratrum viride and mannitol hexanitrate. Mannitol hexanitrate reduces pressure promptly, permitting the veratrum to take effect at a lower pressure level and with lower dosage ... thus reducing possibility of toxic reaction.
2. The G.I. ANTISPASMODIC ACTION of homatropine methylbromide to relax g.i. tension and to prevent or decrease any veratrum nausea.
3. The SEDATIVE ACTION of phenobarbital to allay anxiety and decrease mental tension.

For better and safer control of the many symptoms and the many factors which may aggravate or intensify HYPERTENSION *specify* PERTENAL.

detailed information and samples to physicians on request

CROOKES LABORATORIES, INC. Crookes MINEOLA, NEW YORK

Therapeutic Preparations for the Medical Profession

Zerolo of the Salpetriere Hospital, Paris, describes a simple innocuous way to evaluate the slowdown by a test based on the time elapsing between the instillation of ether into the duodenum and the gustatory perception of the material by the patient.

Using roentgen visualization, an intestinal tube is introduced into the duodenum of the fasting patient and 1 cc. of ether with 5 cc. of normal saline is instilled through the tube. The time is recorded between the injection and the patient's perception of an ether taste on the tongue. Appearance of the ether smell on the breath, though faster, is subject to individual variations and may be confused with ether vapor in the room. A healthy individual tastes the ether after 45 to 50 seconds. If portal circulation is impaired time may increase to about 195 seconds. An arm-to-tongue circulation time, using saccharinate, is performed in each case to determine the status of the general circulation. In cases of cardiac decompensation with hepatomegaly, the portal circulation time is about 85 seconds, the simultaneously performed arm-to-tongue test is approximately 25 seconds, indicating delay not only in portal but also in general circulation.

With alcoholic cirrhosis, the results are from 75 to 140 seconds without ascites, and 110 to 195 seconds with ascites. Liver biopsies show that the severity of the cirrhosis parallels the increase in portal circulation time. Arm-to-tongue tests in these cases are normal, indicating good general circulation. With fatty liver, the portal circulation time remains within normal limits despite lowered liver function.

The permeability of surgical venovenous shunts can be evaluated by the same test.

EAST GERMANY

Hemostasis and Clotting Factors in Different Age Groups. The recalcified clotting time is definitely prolonged with age, finds Dr. Friedrich Horst Schulz of the University of Leipzig, in an investigation of the quantitative relationships of individual components of the clotting mechanism in different age groups. Fibrinogen concentration increases with age; capillary resistance and albumin glomerular ratio decrease. The number of the platelets does not change. These opposite variations are not significant for healthy individuals, but should be recognized for better understanding of the pathologic conditions peculiar to different age groups.

ARGENTINA

Conteben Therapy for Psoriasis. Effects of the thiosemicarbazone compound, Conteben, were studied by Drs. Fernando M. Noussitou and Manuel Seoane of the J. A. Fernández Polyclinic, Argentina, in 22 cases of psoriasis of varying intensity and duration. An initial dosage of 50 mg. orally daily is

(Continued on page 200)

NOW—AN ENEMA THAT'S ADMINISTERED IN **ounces**

INSTEAD OF

PINTS

CLYSEROL 5-MINUTE ENEMA SOLUTION, used both as a retention and a cleansing enema, has proved through four years of clinical testing to be efficient and safe to an outstanding degree, even for heart cases. Since two to four ounces suffice, it obviates painful distention so that patient dread of enemas is quickly overcome.

CANNOT HARM OR IRRITATE MEMBRANES, cannot cause inflammation or toxicity or disturb digestion. This mild solution is non-absorptive and does not interfere with acid base or fluid balance, it evacuates the lower bowel quickly and without undesirable symptoms or discomfort.

TAKES ONLY MINUTES TO ADMINISTER

—usually about five minutes, instead of the usual thirty to forty-five minutes for the average high-fluid enema; an advantage for patient and nurse alike.

DISPOSABLE PLASTIC CONTAINER

is used for only one patient, then discarded; no cleaning-up, no sterilizing before or after administration. May be kept indefinitely without deterioration of solution or container.

for:
PRE & POST-OPERATIVE USE
BARIUM PREP OR IMPACTION
PROCTOSCOPY • OBSTETRICS
INFANTS & AGED PATIENTS
DIVERTICULITIS
STOOL CULTURE
. . . wherever and whenever cleansing of the major bowel is required.

FIRST MAJOR ADVANCE IN ENEMA SOLUTION & METHOD IN A HUNDRED YEARS . . . .

Literature and samples on request

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ENEMA SOLUTION

CONTENTS: Each 100 c.c. contains 1.25 grams Disodium Phosphate and 5.83 grams Monosodium Phosphate

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1533 West Reno, Oklahoma City, Okla.

Relative Blood Concentrations Produced by

SULFONAMIDES

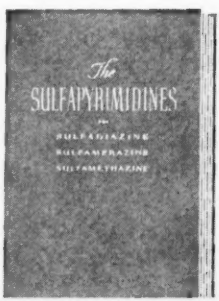
The triple sulfapyrimidine mixture (Meth-Dia-Mer) excels in complete and rapid absorption and in the maintenance of high blood concentrations. Normal doses produce lasting anti-infective blood and tissue levels without frequent repetition.

This triple sulfonamide mixture is being increasingly used by physicians in conjunction with penicillin and other antibiotics.

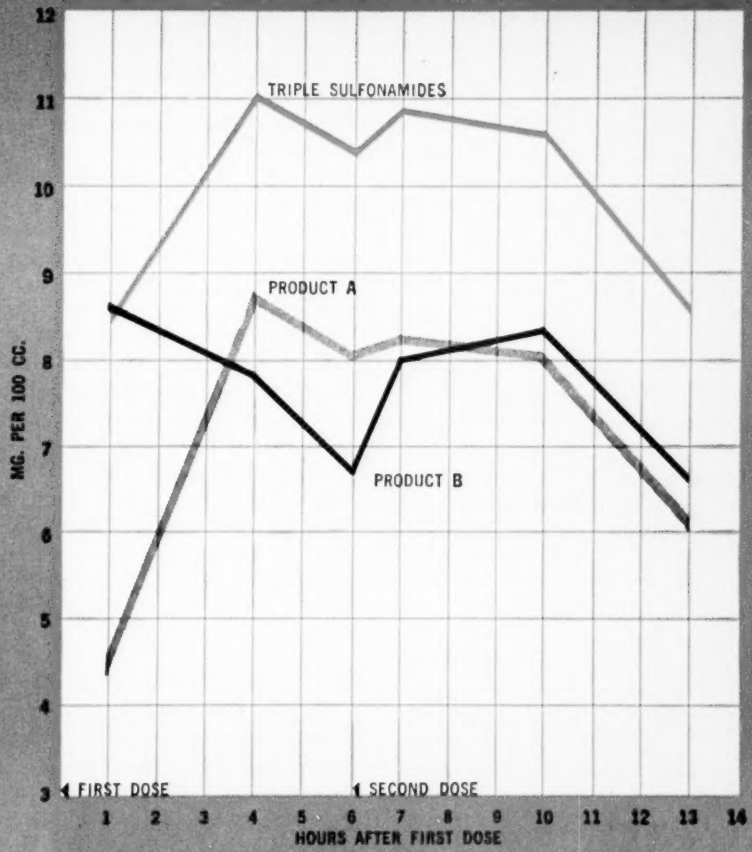
Approximately 13 billion tablets of sulfapyrimidines have been given—intolerance has been very rare.

Have you received your copy of THE SULFAPYRIMIDINES?

This monograph, beautifully leather-bound, may be requested from the detail men of any ethical house calling on you; or, if you prefer, we will send you a copy immediately upon request on your professional stationery.



BLOOD LEVELS OF SULFONAMIDES



Initial dose for all drugs: 4 grams
Second dose 6 hours later: Product A and Product B 2 grams
Triple Sulfonamides 1 gram

This advertisement is presented on behalf of the ethical pharmaceutical manufacturers of Meth-Dia-Mer Sulfonamides by

CALCO CHEMICAL DIVISION
AMERICAN CYANAMID COMPANY Bound Brook, New Jersey

gradually increased to 200 mg. if no sign of intolerance is noted. The area of the lesions was reduced by more than 50% for all but 3 individuals. Lesions cleared completely in 5 cases. Greatest effect appeared within the first two months of treatment. Lesions in the seborrheic regions were the most likely to improve. Untoward reactions to the drug occurred in 4 cases, for 2 of which an error in dosage was responsible. Only 1 patient showed permanent intolerance.

GREAT BRITAIN

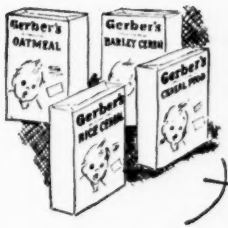
Prevention of Tetanus in Wounded. The British Army Pathology Advisory Committee has recommended that wounded soldiers who have been actively immunized should be given tetanus toxoid and not tetanus antitoxin as before. Brig. A. Sachs reports that an eightfold reduction in the incidence of tetanus was observed in the British army during World War I after the practice of administering prophylactic antitetanus serum to the wounded was adopted. The incidence was lowered during World War II when both active and passive prophylaxis were used. However, in the American army, where toxoid was given for wounding or injury, the incidence was even lower. Present policy in the British army, therefore, calls for active immunization with tetanus toxoid and the use of toxoid for wounding or injury. A primary course of tetanus toxoid is recommended to consist of 2 injections of 1 cc. each, spaced by not less than six or more than twelve weeks. A third injection should be given between six and twelve months after the second injection. These 3 injections are necessary to ensure a satisfactory basal immunity which can be reinforced by booster doses. Unless the third injection is given, a primary course of 2 injections will provide satisfactory titers of circulating antitoxin for only approximately six months. A booster dose of 1 cc. of tetanus toxoid should be given every five years to maintain immunity. However, when wounding or injury in tetanus terrain is likely, an annual booster dose should be given. The administration of tetanus antitoxin may still be necessary [1] when previous active immunization is definitely known not to have been given, [2] in case of multiple injuries, or [3] when surgical attention is considerably delayed after wounding.

GERMANY

Transplacental Transmission of Toxoplasmosis. Serologic studies of maternal and infantile toxoplasmosis show that the number of mothers with positive reactions for toxoplasmosis antibodies is far greater than the number of newborn infants with signs of the disease.

Drs. W. H. Buhn, O. Vivell, and H. Richarz of the University of Freiburg, Germany, believe that positive Sabin-Feldman reactions in the mother and child are no indication that the child has, or will

(Continued on page 204)



For a wholesome beginning

Good carriers for vitamins, minerals

Gerber's Rice, Barley, Oatmeal, and Cereal Food are easily digested . . . carefully supplemented with B-vitamins, calcium, and iron to more than whole grain value.

Less allergenic

Gerber's Rice Cereal and Barley Cereal are both hypo-allergenic. Rice Cereal, Barley Cereal, and Oatmeal are *one-grain* . . . an aid in diagnosing cereal allergies.

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Mother and baby acceptance

Pleasant smooth texture and mild flavors make Gerber's Cereals highly acceptable as starting cereals for infants. Mothers find these pre-cooked cereals convenient . . . easily available in most all grocery stores.

SAMPLES of Gerber's Cereals free for use with patients. Just write on your letterhead to Dept. 215-3, Fremont, Michigan.

Babies are our business . . . our only business

Gerber's BABY FOODS

4 CEREALS • 50 STRAINED & JUNIOR FOODS, INCLUDING MEATS

FACTS ABOUT *Synthetic*

In only five years synthetic detergents have made a tremendous change in the household washing habits of American housewives. At the start of 1948 they accounted for less than 10% of the "laundry soap" business; by the end of 1952 they accounted for over 70%. The product enjoying the greatest popularity in this classification (Tide) is currently being used by one woman out of every four who do their own dishes, and one out of every three who do their own laundry.

For your information the Chemical Division of The Procter & Gamble Company has prepared this article, discussing some of the differences between synthetics and soaps which formerly were widely used.

How synthetic detergents differ from soaps

Synthetic detergents are organic compounds with molecules whose opposite ends are highly polarized like those of soap; one end consists of the type of structure which is oil soluble, the other consists of the type which is water soluble.

Magnesium and calcium soaps formed by interaction of sodium soaps with water hardness are among the most insoluble of compounds. The precipitation which occurs with soap in hard water wastes soap and causes cloudy glassware and unsightly deposits. The "tailor-made" molecules of synthetics do not form these insoluble compounds in hard water. They leave surfaces cleaner . . . free of any precipitated "soap film" formed during rinsing. Also, unlike soaps, in solution, synthetics can be used at almost any pH. Soaps must be kept at pH 10 or above, or they will split into fatty acids. Most synthetic products in general use have solution pHs from 6.0–10.0. Few are above the pH of soap.

The special washing abilities of synthetic detergents

As a consequence of the above characteristics, synthetics are particularly well-suited for washing off acidic soils which would destroy soap. Since they aren't destroyed by hardness or by salts of other metals as soaps are, they are well-suited to washing a great variety of things which could be washed only with alkalis before.

The effect of synthetic detergents on bacteria

The synthetics in general use have about the same effect on bacteria as soaps—that is, some germicidal effect on some strains, but for creating relatively sterile conditions they rely more on removing bacteria than on killing them.

Detergents

The effect of synthetic detergents on skin

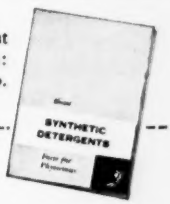
Over the past seven years, Procter & Gamble has included synthetic detergents in the continuing series of tests to measure the effect of washing products on skin. In addition to the routine patch and arm-immersion tests, Procter & Gamble has conducted, under careful medical supervision, extensive clinical and home-usage tests of all its products, including the new synthetics. These tests indicate that household detergents in use today, as a class, do not differ greatly in their effect on the skin from the general-purpose package soaps which have been used for years. Some have a lower pH than soaps and, hence, less effect on persons sensitive to alkali.

Like soaps, the detergents generally are mild primary irritants, but a fact not generally realized is that on the average person subjected to patch or immersion tests, most detergent solutions cause less skin reaction than do soap solutions.

Women have had many years in which to learn whether or not all soaps or certain soaps prove irritating. Problems arising from the effect of soap on skin have, therefore, been spread over decades. In the case of washday detergents, almost every woman in America was exposed to these products in a concentrated period of two or three years.

This widespread use of synthetics, together with their relative newness on the market, have resulted in a situation where synthetics are likely to be suspected as the cause of many cases of dermatitis where they probably are not involved. With almost all housewives now using synthetics for one or more purposes in their homes, it is inevitable that when a physician sees a case of hand dermatitis, a history of exposure to detergents will be obtainable. The significance of the dermatitis must be appraised against the background of the wide use of the detergent products.

FOR FURTHER INFORMATION, send for free booklet, "About Synthetic Detergents — Facts for Physicians." Write: The Procter & Gamble Co., Box 687F, Cincinnati 2, Ohio.



TIDE...

THE SYNTHETIC DETERGENT THAT OUTSELLS ANY OTHER WASHING PRODUCT BY **3** TO **1**!

have, toxoplasmosis. Both mother and child may have high antibody titers without development of toxoplasmosis in the child. If the child does not have congenital toxoplasmosis, the child's titer falls to low nonspecific values or even becomes negative after several months. This fall indicates that the child had transplacental transmission only.

Congenital toxoplasmosis does not exist without a high antibody titer. The persistence of high antibody titers after the fourth month of life is suggestive of congenital toxoplasmosis. A rise in the titer after birth is a sure sign of the disease and is usually accompanied by such indications as fever, malaise, neurologic symptoms, hydro- or microcephalus, chorioretinopathy, and typical calcifications on skull roentgenograms.

High antibody titers in children over 2 years of age, with or without clinical evidence of the disease, can be considered indicative of acquired toxoplasmosis; lack of antibodies in the mother confirms the diagnosis of the acquired form.

2

Electroencephalography in Eclampsia. Electroencephalographic changes are found in eclampsia only during and after the status eclampticus. In these periods the electroencephalogram is very similar to that seen with epilepsy, report Dr. R. Janzen and associates of the University of Hamburg-Eppendorf.

In true eclampsia, the abnormalities disappear within one to three weeks, an important observation in the differential diagnosis between eclampsia and epilepsy. During preeclampsia, as well as immediately before the first attack, no electroencephalographic alterations can be found, even after such provocations as the flicker test and hyperventilation are used.

The lack of evidence of functional cortical abnormalities does not preclude changes in other areas of the brain.

3

Hormones for Liver Disease. Adrenocortical steroids, by beneficial action on the metabolic disturbances involved, reduce the duration and gravity of epidemic or homologous serum hepatitis, asserts Dr. Günter P. Albus of the Academy of Medicine, Düsseldorf.

Best results are obtained when total adrenocortical extract is given with dextrose. The patient's general condition improves quickly and the serum bilirubin falls readily to 50 or even 30% of pretreatment values, often within several hours. No side reactions appear unless the dose is excessive.

When cortisone is given alone, the jaundice decreases initially, but relapse and deterioration occur as soon as administration is discontinued. Desoxycorticosterone acetate (DOCA) given alone not only fails to produce the desired effect but causes a rise in blood pressure and increases electrolyte imbalance. Furthermore, prolonged administration of DOCA may cause pituitary inhibition and adrenocortical exhaustion.

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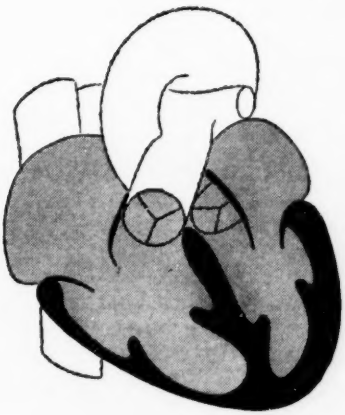
the first intramuscular digitoxin

DIGITALINE NATIVELLE® INTRAMUSCULAR

for dependable digitalization and maintenance when the oral route is unavailable



DIGITALINE NATIVELLE INTRAMUSCULAR
is indicated for patients who are comatose, nauseated or uncooperative, or whose condition precludes the use of the oral route.

DIGITALINE NATIVELLE INTRAMUSCULAR
provides all the unexcelled virtues of its parent oral preparation.

Steady, predictable absorption.

Equal effectiveness, dose-for-dose with oral DIGITALINE NATIVELLE.

Easy switch-over to oral medication.

Clinical investigation has shown that DIGITALINE NATIVELLE INTRAMUSCULAR is "effective in initiation and maintenance of digitalization. A satisfactory therapeutic effect was obtained with minimal local and no undesirable systemic effects."*

DIGITALINE NATIVELLE INTRAMUSCULAR – 1-cc. and 2-cc. ampules; boxes of 6 and 50. Each cc. provides 0.2 mg. of the original digitoxin – DIGITALINE NATIVELLE.

*Strauss, V.; Simon, D. L.; Iqlauer, A., and McGuire, J.: Clinical Studies of Intramuscular Injection of Digitoxin (Digitaline Nativelle) in a New Solvent, Am. Heart J. 44:787, 1952.

Literature and samples available on request.

VARICK PHARMACAL COMPANY, INC.
(Division of E. Fougera & Co., Inc.)
75 Varick Street, New York 13, N. Y.

LATE REPORTS *from Medical Centers*

★ UNIVERSITY OF CALIFORNIA, Los Angeles--Plasma may be obtained from the same people more often and in much greater amounts if red cells are separated and injected into donors. No ill effects result from increased withdrawal if those giving blood are fed a diet high in protein and calories. Dr. John S. Lawrence and associates suggest that plasma for stockpiles could be furnished only by small, carefully selected groups, to prevent transmission of infections such as viral hepatitis.

★ WALTER REED ARMY HOSPITAL, Washington, D. C.--An accurate test for calcium in blood or urine may be completed by flame spectrophotometry within minutes after withdrawal of a small sample. About 25 determinations can be done in one hour. The method adopted by Drs. Alfred D. Winer and Dwight M. Kuhns has also been employed for sodium and potassium determinations.

★ SANTA CLARA COUNTY LABORATORY OF CRIMINALISTICS, San Jose, Calif.--Poisons, narcotics, and other organic compounds are quickly identified by a technic utilizing the spectrophotometer. James W. Brackett, Jr., and Lowell W. Bradford employ the Stas-Otto principle to separate unknown material into acid, alkaline, and neutral groups before examination. Light patterns are transcribed on special graph paper and compared with standard forms. Tests may be useful in diagnosis of unusual illness, analysis of foods and drugs, and murder and suicide investigations.

★ UNIVERSITY OF OREGON, Portland--Color of human skin may be controlled and blemishes such as those occurring in vitiligo corrected by use of psoralens and the monobenzylether of hydroquinone, assert Drs. A. Bunsen Lerner and Thomas B. Fitzpatrick. Factors affecting human pigmentation include diet, sunlight, hormones, and aging. By employment of hormones to duplicate what appears to be body chemistry, isolated frog skin can be colored and decolored.

★ MASSACHUSETTS INSTITUTE OF TECHNOLOGY, Cambridge--The 2,000,000-volt roentgen ray generator is surpassing expectations for treatment of cancer, report John Trump and Dr. Hugh F. Hare. No sign of the disease can be found in 293 of the 455 cancer patients treated between October 1949 and October 1952. Many cases were far advanced and refractory to other methods.

★ UNIVERSITY OF ROCHESTER--An unnamed enzyme discovered in tumor tissue of rats indicates that neoplasms may have unique biochemical characteristics. Drs. Elmer H. Stotz and Fred V. Lucas and Harold A. Neufeld isolated the substance while investigating hormonal influence in metabolism. Apparently lacking in adult tissues, the enzyme occurs in the embryo at early stages but vanishes before birth.

★ HARVARD UNIVERSITY, Boston--Pure alkaloids of Veratrum may soon be isolated on a large scale, with the aid of a technic announced by Drs. S. Morris Kupchan and C. V. Deliwala. In the process of separating such compounds as neogermitrine and germitetrine, chromatography is substituted for the stage of counter-current distribution. Pure crystalline products may eliminate animal assay in standardization of hypotensive drugs.

BASIC SCIENCE *Briefs*

Virology

Tissue Culture of Poliomyelitis Virus

Human embryonic brain, cord, or kidney tissue is combined with a synthetic nutrient medium, mixture No. 199, to propagate the Lansing poliomyelitis virus in culture. Prolongation in survival of tissue fragments and greater liberation of virus into the supernatant fluids result when the mixture is used in preference to Hanks-Simms' medium. High titers of the virus are demonstrable by mouse inoculation even after one hundred days of test-tube life, report Dr. A. E. Franklin and associates of the University of Toronto and the Hospital for Sick Children, Toronto. The mixture also has advantages over media containing animal organ extracts and serum, since the nutrient is well defined chemically and contains no animal antigens. This culture method can lead to mass production of large quantities of poliomyelitis virus for use in vaccines, skin tests, or physicochemical studies.

Canad. J. M. Sc. 31:64-74, 1953.

"H - O - T - E - L"

Hormones

Tubal Ligation and Ovarian Function

The periovarial sac appears to be a collector of capsular fluids which aid in the passage of the ovum to the uterus and is not primarily a barrier to estrogenic escape into the peritoneum. Bilateral ligation of rat oviducts proximal to the uterus results in a greatly distended capsule containing estrogen, but vaginal smears show prolonged periods of estrus, indicating estrogenic stimulation of the endometrium. Therefore, Dr. Cornelius A. Navori and associates of the University of Chicago believe the route of estrogenic hormone from the ovary to the uterus is more complicated than a direct passage through the oviduct, although some of the hormone undoubtedly travels the direct route. Removal of the ovarian capsule in operated animals results in resumption of normal estrous cycles.

Proc. Soc. Exper. Biol. & Med. 81:649-652, 1952.

antibacterial activity of penicillin and dihydrostreptomycin synergistically combined for greater therapeutic efficacy and convenience in

Combiotic®

providing both antibiotic agents for treatment of certain mixed bacterial infections, particularly urinary tract infections, penicillin-resistant gonococcal infections, complications of upper respiratory infections and other infections caused by susceptible organisms.

Pfizer world's largest producer of antibiotics

Supplied as

Combiotic Aqueous Suspension *in 5-dose (10 cc.) drain-clear vials containing 400,000 units penicillin G procaine crystalline and 0.5 Gm. dihydrostreptomycin sulfate in each dose*

Steraject* *Combiotic Aqueous Suspension single-dose disposable cartridge*

Combiotic P-S (dry powder) ***1.0 Gram Formula*** *containing in each dose 300,000 units penicillin G procaine crystalline, 100,000 units buffered penicillin G sodium crystalline plus 1.0 Gm. dihydrostreptomycin sulfate*

Combiotic P-S (dry powder) ***New 0.5 Gram Formula*** *containing 300,000 units penicillin G procaine crystalline, 100,000 units buffered penicillin G sodium crystalline plus 0.5 Gm. dihydrostreptomycin sulfate*

Antibiotic Division
Chas. Pfizer & Co., Inc.
Brooklyn 6, N. Y.

*TRADEMARK, CHAS. PFIZER & CO., INC.

A new case history with photographs

The unique value of 'Dexamyl' in providing symptomatic relief from mental and emotional distress is clearly demonstrated in this case history—reported by a general practitioner.

Patient: C.P. (shown in photos on opposite page), age 38, undergoing an early menopause. "She once said, 'You know, Doctor, my children and husband ought to hate me. I yell and shriek and throw things. If it weren't for cigarettes and coffee I think I'd go crazy. There's not a place in my body that don't hurt me ... my head, my heart, my belly ... but oh, my nerves!' Her kind and understanding husband—a retired navy gunner—experienced more violent battles in his bedroom than he ever saw at sea."

Medical Treatment: 'Dexamyl', one tablet t.i.d. for 5 weeks; then ½ tablet t.i.d. for 13 weeks; and now ½ tablet p.r.n. Also, adjuvant estrogen therapy.

Response: 'Dexamyl' provided "... sedation without depression; elation without euphoria. She recently told me, 'These green heart-shaped pills ... they carry me along without my coffee pot and my cigarette case. They make me feel like I'm all right and the world isn't hard to live in. My boy just said a whole week went by without me hollering at him.'"

Dexamyl* tablets and elixir

to relieve anxiety, depression and inner tension

Each tablet contains Dexedrine* Sulfate (dextro-amphetamine sulfate, S.K.F.), 5 mg.; amobarbital (Lilly), ½ gr. Each 5 cc. teaspoonful of the elixir is the dosage equivalent of one tablet.

Smith, Kline & French Laboratories, Philadelphia *T.M. Reg. U.S. Pat. Off.

These unposed photographs of patient C.P. were snapped during an actual interview with her physician. See the opposite page for the case history of this patient.

short REPORTS

Anticoagulants

Effects of Indandione Derivative on Clotting

Dipaxin (diphenylacetyl-1, 3-indandione) has a significant hypoprothrombinemic effect in man. The anticoagulant is active in single doses of as little as 4 mg., thus more potent than dicumarol on a weight basis. Single doses of 20 mg. result in marked hypoprothrombinemia after forty-eight hours and the effect lasts six to ten days. Dr. John B. Field and associates of the University of Southern California, Los Angeles, administer the drug to patients with acute myocardial infarction, suspected infarction, myocardial insufficiency, pulmonary embolism, and thrombophlebitis. A starting dose of 20 mg. is used, followed by daily doses of 2 to 4 mg. to maintain adequate levels of prothrombin. Vitamin K readily overcomes the anticoagulant effect. Although 15 to 25 times more effective than dicumarol, Dipaxin takes longer to produce hypoprothrombinemia, and return to normal is delayed.

Proc. Soc. Exper. Biol. & Med. 81:678-681, 1952.

"See if you can hear anything!"

Hematology

Polycythemia Vera Therapy

Triethylenemelamine acts similarly to nitrogen mustard, radioactive phosphorus, and radiation by depressing erythropoiesis in treatment for polycythemia vera, report Dr. Rose Ruth Ellison of Memorial Center for Cancer and Allied Diseases, New York City, and associates. Daily oral doses of 5 mg. were given to 6 patients for four days; further dosage for five to thirteen additional months varied from 10 to 20 mg. per course, with dose and frequency of administration dependent upon individual symptoms and blood studies. All patients had significant diminution of hematocrit volumes, 3 had complete symptomatic relief, and 2 had some amelioration of symptoms. Severe nausea and vomiting were noted in ! case.

Cancer 6:327-332, 1953.

Knox Gelatine proven effective in the treatment of Refractory Anemias

Recent investigation shows[1] hemoglobin concentration and red blood cell count increased in every case, with high statistical significance, in refractory anemia patients plateaued to iron and getting a good diet.

Gelatine is a good hematopoietic protein because it contains 70 per cent of blood-building amino acids, according to criteria of Whipple and Robscheit-Robbins.[2]

Gelatine contains 25 per cent of glycine, an amino acid used in the synthesis both of the hemin[3] and the globin[4] portion of hemoglobin, and is utilized directly for these purposes.[5]

AVAILABLE AT GROCERY STORES IN 4-ENVELOPE FAMILY SIZE AND 32-ENVELOPE ECONOMY SIZE PACKAGES.

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Knox Gelatine U.S.P. • All Protein • No Sugar

1. Reich, C., and Mulinos, M. G., Treatment of Refractory Nutritional Anemia with Gelatine. Bull. N. Y. Med. Coll. March 1953.

2. Whipple, G.H., and Robscheit-Robbins, F.S.: Amino Acids and Hemoglobin Production in Anemia, J. Exper. Med. 71:569, 1940.

3. Shemin, D., and Rittenberg, D.: Utilization of Glycine for the Synthesis of the Porphyrin, J. Biol. Chem. 159:567, 1945; The Biological Utilization of Glycine for the Synthesis of the Protoporphyrin of Hemoglobin, J. Biol. Chem. 166:621, 1946.

4. Grinstein, M., Kamen, M., and Moore, C.V.: The Utilization of Glycine in the Biosynthesis of Hemoglobin, J. Biol. Chem. 179:359, 1949.

5. Graff, J., and Hoverman, H.D.: On the Metabolism of Beta-Alanine, J. Biol. Chem. 186:369, 1950.

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A recent clinical evaluation* of the effectiveness of certain drug combinations in acute upper respiratory infections, including the "common cold," clearly demonstrated A-P-Cillin to be, by far, the superior preparation.

It was found that 97.5% of the patients receiving A-P-Cillin were completely asymptomatic or improved at the end of the 72 hour treatment period.

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Each tablet contains:

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	Phenacetin	2 gr.
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The usual adult dose of A-P-Cillin is 2 tablets administered three times per day. Clinical experience indicates that treatment should be continued for not less than seventy-two hours. For optimal effect, the tablets should be taken at least one hour before or two or more hours after meals.

White Laboratories, Inc., Kenilworth, N. J.

*McLane, R. A.: Clinical Evaluation of Combined Drug Therapy in Acute Upper Respiratory Infections, J. M. Soc. N. J. 49:509 (Dec.) 1952.

Awards

Rheumatology Prize

A competition for the best original unpublished article on the nature and treatment of rheumatic and arthritic diseases is sponsored by the Italian Society of Rheumatology. A prize of 1,000,000 lire is offered. Inquiries may be sent to Azienda Autonoma di Cura, Acqui, Piemonte, Italy. Entries must be received by the society by Jan. 31, 1954.

Antibiotics

Treatment for Nephrosis

Remissions of the nephrotic syndrome are induced by the interrupted use of ACTH and cortisone. ACTH, 100 mg. daily for seven days, promotes temporary diuresis and a concomitant rise in serum complement levels to normal. Five to seven days after initial treatment, 100-mg. doses of the drug are given daily for three consecutive days; this procedure is repeated weekly for five to eight weeks. Oral cortisone, 100 mg. four times a day, can be substituted in the interrupted schedule with equally successful results, report Dr. Kurt Lange and associates of New York Medical College, New York City. Of 6 patients treated by this method, 3 have no laboratory evidence of the disease, while the others show some chemical alterations in urine and blood. All are edema free and have normal serum complement values.

Proc. Soc. Exper. Biol. & Med. 82:315-317, 1953.

Cardiology

Pulmonary Arterial Pressure

Nervous stimuli may contribute to pathogenesis of pulmonary hypertension and control occurrence of paroxysmal nocturnal dyspnea and pulmonary edema, report Dr. D. Halmágyi and associates of University Medical School, Szeged, Hungary. Sleep, tetraethylammonium bromide, and Dibenamine will decrease pulmonary pressure and resistance in heart failure by relieving the neurogenic vasoconstrictor tone. However, administration of dihydroergotamine increases pulmonary arterial systolic pressure and resistance by constricting pulmonary vessels. Sodium nitrite abolishes the effects of pulmonary hypertension caused by dihydroergotamine. The action of sodium nitrite, a drug dilating only constricted vessels, suggests existence of pulmonary vasoconstriction in heart failure.

Brit. Heart J. 55:15-24, 1953.

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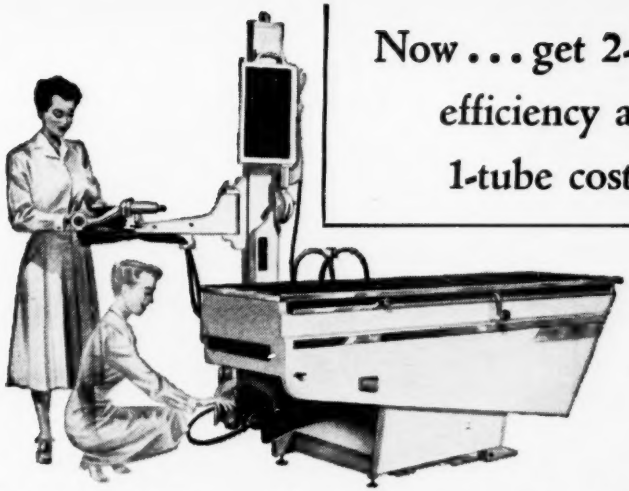

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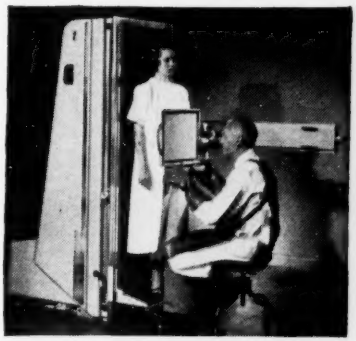

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S. C. Freed, M. D.—Newer Concepts in Treating Obesity, GP, Vol. VII, No. 1, Jan. 1953

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Drugs

Gastrointestinal Motility

Banthine decreases gastric motility to a greater extent than does belladonna. A striking delay in gastric evacuation and decrease in movement of barium down the intestine occur when 100-mg. doses of Banthine are given orally to healthy subjects, report Dr. William P. Chapman and associates of the Massachusetts General Hospital and Harvard University, Boston. The barium method, employed to compare Banthine, tincture of belladonna, and placebos, reveals belladonna to be only slightly more effective than placebos in delaying gastric motility. Results of tests for gastric evacuation are the same for both placebos and belladonna. Untoward reactions from the drugs are slight, with mouth dryness and sore throat the commonest.

Gastroenterology 23:234-243, 1953.

Rehabilitation

False Wall for Rocking Beds

To make reading easier for poliomyelitis patients confined to rocking beds, a false wall, complete with wallpaper and hung pictures, may be attached to the end of the bed. The wall rises and falls with the bed, thus eliminating the distraction caused by regular room walls which appear to oscillate when the patient reads.

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Experimental Medicine

Leukemogenic Agent

Cell-free extracts of leukemic mouse tissue are capable of inducing leukemia when injected into newborn mice of another inbred line. Specimens of leukemic spleens, livers, and nodes of Ak mice, centrifuged at 9,500 rpm for fifteen minutes, are inoculated into newborn mice of the genetically different C3H line. The apparently cell-free supernatants induce the cancerous blood disease within five months in 46% of inoculated animals, reports Dr. Ludwik Gross of the Veterans Administration Hospital, Bronx. If the same inoculum is heated before injection, all animals remain in good health. Centrifugation at 44,000 rpm for two and one-half hours appears to settle out the agent, since the supernatant becomes ineffective while the sediment induces a high percentage of leukemias. The induced disease in the C3H mice is readily transplantable into other adult C3H mice, but not into Ak animals, even though the original donor tissue came from the Ak strain. The experiment suggests the presence in mice of a specific, thermolabile, transmissible leukemogenic agent of an unknown nature.

Cancer 6:153-158, 1953.

Cardiac Surgery

Heart Transplantation

Homologous transplantation of dog hearts is possible with the aid of hypothermia. Lowering temperature to 21 to 24° C., Dr. Wilford B. Neptune and associates of Hahnemann Medical College, Philadelphia, stop all circulation for approximately fifteen minutes, remove recipient animal's heart and lungs, and substitute a donor heart-lung complex. Partial circulation, to preserve the central nervous system, is accomplished by immediate connection of the donor aorta and superior vena cava to the corresponding vessels of the recipient. Polyethylene tubing is utilized to make connections until careful suturing can be done. Junction of the inferior vena cava completes circulation, and the remaining anastomoses of the trachea and cavae are performed once cardiac function becomes adequate. Donor hearts transplanted into 3 animals were found to maintain successful circulation up to six hours postoperatively, with a return of reflexes, spontaneous respiration, and normal temperature.

Arch. Surg. 66:174-178, 1953.

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References: 1. Schwartz, J.: *Furacin Vaginal Suppositories in Pre- and Postoperative Treatment of Cervix and Vagina,* Am. J. Obst. and Gynec. **63**:579 1952 • 2. Doyle, J. C.: *Vaginal Infections and Their Management,* Urol. & Cutan. Rev. 55:618, 1951.

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*Beckman, H.: Pharmacology in Clinical Practice, Philadelphia, W. B. Saunders Company, 1952, p. 361.

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Pharmacology

Drug for Malaria

Daraprim delays the incubation period of *Plasmodium cynomolgi* in monkeys but does not eradicate underlying tissue stages. The drug, 2,4-diamino-5-p-chlorophenoxy-pyrimidine, is administered in daily doses of 0.075 to 20 mg. per kilogram of body weight for eight days after inoculation with sporozoites. In established disease, peripheral parasitemia is abolished and the interval between treatment and relapse is prolonged. Given in the amount of 0.15 mg. per kilogram of body weight once weekly, Daraprim is 10 to 20 times as active as chlorguanide and 100 times as effective as chloroquine. In trophozoite infestation 0.0024 mg. per kilogram of body weight of the drug daily effectively reduces the number of parasites in the blood. Because of slowness of action and potentiality for producing resistance, Daraprim is most useful prophylactically as a routine suppressive, believe Drs. L. H. Schmidt and Clara S. Genther of Christ Hospital Institute of Medical Research, Cincinnati.

J. Pharmacol. & Exper. Therap. 107:61-91, 1953.

When Chronic-Fatigue, Insomnia are due to Low Blood Sugar Level...

Prescribing a simple change in diet may often restore energy and zest for living in many patients.

THE pace of modern living . . . business pressures, strenuous social activities, hurried meals, improper diet . . . all too frequently lead to exhaustion, loss of energy, inability to sleep. Now clinical studies show that these clinical manifestations are often associated with hyperinsulinism—causing a lowered *blood sugar level.**

Portis reported these fatigue states were aggravated when the patients consumed beverages and foods that contained free sugar. He further stated that while these raise the blood sugar level momentarily, their "free" sugar is burned up too quickly, and a greater letdown follows. On the basis of this evidence a diet high in proteins and relatively high in carbohydrates in a complex form was given to his patients. He found such foods as milk are especially beneficial because they are digested more slowly, and because they maintained the blood sugar level for a longer period.

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*Portis, Sidney A., Life Situations, Emotions and Hyperinsulinism, J.A.M.A. **142:** 1281-1286 (April 22) 1950.

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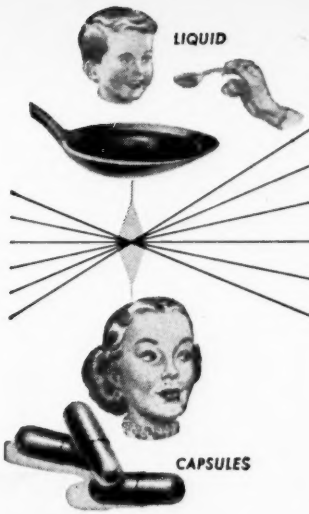

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Biotin	0.02 mg.
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Pruce, A. M.: J. Med. Ass. Georgia 40: 101, 1951

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SULPHOCOL SOL for parenteral use in 25 cc. multiple-dose vials and boxes of 12-2 cc. vials. Dose: Ascending doses every 3 to 7 days starting with 0.25 cc.

SULPHOCOL—Colloidal Sulfur Compound—meets these requirements. By its detoxifying action it reduces joint swelling and thus lessens pain; further joint involvement is prevented or minimized. It is comparatively inexpensive. Moreover, it is safe.

Over a period of years SULPHOCOL has given gratifying relief to thousands of arthritis patients. Clinical experience is ample proof of the efficacy and safety of this form of therapy. It has stood the test of time.

Write for literature and sample of Sulphocol Capsules.

SULPHOCOL®

Colloidal Sulfur Compound

Oral and Parenteral

MULFORD COLLOID LABORATORIES

A PRODUCT OF THE MULFORD COLLOID LABORATORIES

THE NATIONAL DRUG COMPANY, PHILADELPHIA 44, PA.

More Than Half a Century Service to the Medical Profession

Honest Answer

A small boy was awaking from his tonsil anesthetic. The anesthetist asked him how he felt.

"I never had so much trouble in all my life," he wailed.—J.M.H.

Unsuited

My small daughter received her first lesson in genetics recently and asked the following question: "Daddy do you know why I don't have blue eyes?" Her interest pleased me but her answer came as a shock:

"Because you have the wrong kind of pants."—H.R.K.

He Chose The Better Part

As an office receptionist, I meet some difficult people. Not often do I get a chance to dig back with a truthful answer that serves as a squelcher. Recently, however, an elderly dowager was being very difficult.

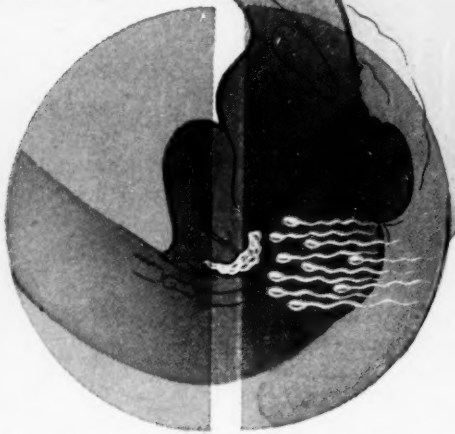
"I've told you my name and address and the hour of my appointment," she said looking down her nose. "Now, if you'll kindly tell the doctor I'm here, I'm sure he'll display more sense than you have."

"He already has," I replied with my nicest smile. "He went out as soon as he saw you come in."—A.S.

"I'm writing a book on what to do until the patient comes."

INDEX TO ADVERTISERS

RAPID IMMOBILIZATION Plus OPTIMUM BARRIER ACTION



Clinicians of the widest experience in conception control hold that two properties are essential in contraceptive jellies:

1. The product must immobilize sperm rapidly
2. The product must provide complete occlusion of the cervix for a sufficient number of hours

Whenever pelvic examination establishes that conception control with jelly alone will provide adequate protection, there is no better product than RAMSES* Vaginal Jelly. Continuous tests conducted by an independent accredited research laboratory establish that RAMSES Vaginal Jelly immobilizes sperm in the fastest time recognized under the Brown and Gamble technic. Direct-color photographs show that the cervix remains occluded far beyond the survival time of sperm in the vagina.

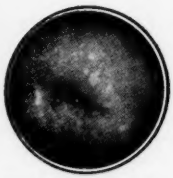


Fig. 1. Photo taken after insertion of RAMSES Vaginal Jelly. Os occluded.

Fig. 2. Photo taken ten hours after coitus. Occlusion still manifest.

Jelly stained with non-spermatocidal concentration of methylene blue for photographic purposes.

RAMSES Vaginal Jelly is offered for use only under the guidance of the physician.

Ramses® VAGINAL JELLY

gynecological division

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423 West 55th Street • New York 19, N.Y.
quality first since 1883

*Active ingredients, by weight: Dodecaethyleneglycol monolaurate 5%; boric acid 1%; alcohol 5%.

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peptic ulcer
patients . . .

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bromide

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New High Potency
Anticholinergic with
No Bitter Aftertaste

As adjunctive therapy in your standard peptic ulcer regimen*, Antrenyl offers potent anticholinergic action to inhibit motility of the gastrointestinal tract and gastric secretion.

Although Antrenyl is one of the most potent of all anticholinergic agents, it rarely causes esophageal or gastric irritation and has no bitter aftertaste. In individualized doses, it is well tolerated and side effects are absent or generally mild.

In one study[1] patients receiving Antrenyl obtained relief from acute symptoms within 24 to 36 hours. Dosage was individually adjusted at 5 to 10 mg. four times a day. Side effects were adjudged less pronounced than those of other similar agents ordinarily used in the management of peptic ulcer.

Prescribe Antrenyl in your next case of peptic ulcer and spasm of the gastrointestinal tract. Available as tablets, 5 mg., scored, bottles of 100; and syrup, 5 mg. per teaspoonful (4 cc.), bottles of 1 pint.

Ciba Pharmaceutical Products, Inc., Summit, N. J.

**Leading gastroenterologists recommend:*

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sedation
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1. Rogers, M. P., and Gray, C. L.: *Am. J. Digest. Dis.* 19:180, 1952.

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